SURGERY

VOL. 3 APRIL, 1938 NO. 4

Original Communications

SOME ACCOMPLISHMENTS OF THORACIC SURGERY AND ITS PRESENT PROBLEMS*

EVARTS A. GRAHAM, M.D., ST. LOUIS, MO.

(From the Department of Surgery, Washington University School of Medicine and Barnes Hospital)

IT IS an honor to be invited to give the lecture named in honor of Edward Starr Judd. To a remarkable degree he combined those qualities which one would readily ascribe to the ideal surgeon, remarkable clinical judgment, masterful operative technique, an inquiring mind eager to solve some of the baffling problems of our profession, humane gentleness and kindliness in dealing with those distressed and worried by their illness, the ability to inspire others less gifted to attempt to reach to the stars. It is a pleasure to be able to pay this brief tribute to him. I am one of many who admired him and who were inspired by him.

Forty-one years ago (1896) there appeared the first extensive book devoted to thoracic surgery. This work, by Stephen Paget,[1] contains the following statement: "It is sometimes said that surgeons fifty years hence will think as little of our results as we think of the methods of fifty years ago. So far as regards the surgery of the chest, this is utterly untrue. Fifty years ago, it had risen above the horizon, it is now nearly at its zenith. Indeed, it is possible that we may see its upward movement checked."†

Nearly fifty years have now elapsed since that statement was made, and it seems fitting that those of us who are now particularly interested in thoracic surgery should take stock of what has been accomplished. Paget's scholarly book makes a serious attempt to present the status of this branch of surgery throughout the world at the time. In order to have a proper basis, therefore, of comparing the field of thoracic surgery

*Judd Lecture, presented on February 3, 1937, at the University of Minnesota Medical School, Minneapolis, Minn.

†Truc's monograph in French had appeared in 1885, "Essai sur la chirurgie du Poumon," Paris, 1885, but it was not nearly so extensive as Paget's book.

Received for publication, January 3, 1938.

in the year 1937 with that in the year 1896, let us pause briefly to review the book. For the most part this work of 479 pages deals with the surgical treatment of conditions of the chest wall, such as injuries of various kinds, malformations, tumors, etc. Empyema and other pleural effusions, however, receive much attention. So far as the lung itself is concerned, surgical intervention at the time consisted chiefly apparently of opening cavities for external drainage, whether they were of pyogenic or tuberculous origin. Mention is made of the cases of Tuffier and of Lowson in which in two patients the apex of the lung was successfully removed for tuberculosis. However, Paget condemns the operation and even mentions the incident of the suicide of an unnamed surgeon following an unsuccessful attempt to remove both apices in a case of tuberculosis. How often have many of us surgeons felt inclined to follow that example when death has unexpectedly and tragically intervened to block our efforts to restore a patient to health by an operation! The accepted method of treating mediastinal tumors was by drainage if they were cystic, but otherwise no operation was considered advisable. The recognized surgical conditions of the heart were pericardial effusions of various kinds. No case of successful suture of a wound of the heart was known to Paget. Indeed the first one was that of Rehn which was published in the same year as the appearance of Paget's book. Roberts,[2] of Philadelphia, a better prophet than Paget, fifteen years previously, however, had predicted that the time might come when the heart muscle would be sutured in some cases of wounds. Elkin's[3] recent publication of his seven successes in thirteen cases of sutured heart wounds is a confirmation of that prophecy.

Probably it is easier to be a historian than a prophet. At any rate it is apparent to anyone today that Paget was about as wrong as possible in his prophecy despite the fact that he probably had a more scholarly knowledge of thoracic surgery than anybody else of his time.

The most important factor in retarding the development of chest surgery seems to have been the fear of entering the free pleural cavity. The danger of death from open pneumothorax was a matter of common knowledge to the ancient Greeks, and it has been only during the last twenty years or less that practical and adequate safeguards have been developed to prevent the serious consequences of operating within a free pleural cavity. The Great War furnished numerous examples of the possibility of operating within the pleural cavity to remove missiles of various kinds, and an entirely unjustified impression became prevalent that the danger of open pneumothorax had been greatly overestimated. Some even concluded that operations could be performed within the pleura with the same impunity as within the abdomen. Careful studies showed, however, that although such a conclusion was erroneous, nevertheless individuals with a relatively high vital capacity (for example, 5,000 c.c. or above) could withstand for a short time a large opening in

the chest wall.[4] On the contrary, in those with a low vital capacity a much smaller opening would prove fatal unless the mediastinum were stabilized to a sufficient extent to prevent its shifting. The introduction of the factor of the vital capacity and its relation to the size of the opening which could be tolerated by the patient gave us a much clearer understanding of the whole question. The practical solution of the problem which has really made possible a fearless entering of the thorax for surgical procedures has been the development of intratracheal and of intrapharyngeal anesthesia which permits the rhythmic inflation and consequent aeration of the lung under positive controlled pressures. Probably to Meltzer and Auer belongs the chief credit for the development of this type of anesthesia although various pioneers preceded them. But even this very practical aid to operating within the chest did not come into general use until the reasons for it had been forcefully brought to attention by the experiences in the Great War and the physiologic studies which came out of it.

Another important factor in the retardation of thoracic surgery was the lack of precise diagnosis of intrathoracic conditions. The development of the use of the x-ray to its present remarkable state of accuracy could hardly have been predicted by Paget in 1896, for Roentgen had announced his discovery in only the preceding year. Again the invention of direct bronchoscopy by Killian, of Mainz, in 1898 has been of enormous assistance in perfecting the diagnosis of lesions within the tracheobronchial tree and in the treatment of some intrathoracic conditions.

It will not be possible in the course of a single lecture to discuss extensively the surgical accomplishments which have followed the fundamental discoveries just mentioned. Let us, however, examine some of them. Let us begin with empyema, perhaps the first of the intrathoracic conditions recognized as best treated by surgical methods. Two principles in the treatment of this condition seem now to be firmly established, of which one is that empyema is essentially a surgical disorder demanding surgical drainage in nearly all cases. The other principle is that open drainage during the developmental stage is fraught with so much danger to the life of the patient that it should not be undertaken. Until the time comes when specific therapy against the infecting organisms is at hand it seems probable that these two principles will stand. They were recognized empirically by Hippocrates but because the underlying rationale of them was not understood until the period covered by the last two decades they were largely lost sight of. The terror of the epidemic which afflicted the United States Army camps in 1917 and 1918 was increased by the fact that many needless deaths occurred because the surgeons believed that early open drainage should be induced even before the inflammatory reaction had developed into an abscess. We now know that empyema in itself rarely causes death. The deaths which occur are due almost entirely to the pneumonia of which the empyema

is only a complication or to the unwise creation of an open pneumothorax for drainage purposes during the period of active pneumonia. The particular danger to the patient lies in the fact that at that period of the disease his vital capacity may be only slightly greater than the tidal air requirement. The danger of death from asphyxia is therefore very great if the respiration is embarrassed still more by the presence of an open pneumothorax. Various improvements in the technique of drainage and in other particulars which have been introduced in recent years are distinct advantages. Closed drainage, to mention only one, is one of them. These matters, however, are essentially details which the limitation of time will preclude my discussing. After all it is the principles in which we are most interested. Because of the establishment of the two principles mentioned, future epidemics of influenza associated with empyema are not likely to terrify us so much as did the last great epidemic.*

When we consider the lung we find that the situation has been revolutionized. This revolution concerns not only our conceptions of what constitutes surgical pulmonary conditions and improved methods of treating them but even in some instances our fundamental ideas of the conditions themselves. Abscess of the lung is a good example which shows the progress which has been made. Our understanding of this disease has been enormously clarified by the studies which have shown that probably in the majority of instances it is the result of the aspiration of the proper sort of infectious material into the lung combined with an inability to cough it out, although in some cases embolism is undoubtedly the responsible etiologic process. Again, probably in the majority of cases, the organisms which are chiefly important are various putrefactive anaerobes which inhabit the mouth and are particularly likely to be associated with pyorrhea alveolaris. Many such organisms have from time to time been incriminated, spirochetes and fusiform bacilli of various kinds and more recently the *Bacterium melaninogenicum* (Burdon, K. L.,[5] and Varney, P. L.[6]). The chief etiologic significance of this knowledge is that operations in dirty mouths under general anesthesia, which both increase the risk of aspiration and reduce the expulsive cough, carry a special danger of the development of a pulmonary abscess as a complication. Application of this knowledge by the laryngologists within recent years seems greatly to have reduced the number of cases of lung abscess. The diagnosis, through the assistance of the x-ray and the bronchoscope, has been vastly improved. Likewise the therapy has been advanced. We know now that in many positively diagnosed acute cases spontaneous cures occur by the use of such simple measures as postural drainage and bronchoscopy. Surgical drainage is used boldly in those cases in which improvement seems not to be occurring promptly.

*It seems probable also that the use of sulphanilamide in the streptococcal cases may prove to be very beneficial.

In the field of pulmonary tuberculosis the results of properly applied surgical measures would doubtless seem incredible to Paget and his contemporaries. To Brauer and Friedrich belongs most of the credit for planning and initiating the modern operation of extrapleural thoracoplasty, although this operation has been greatly modified since their time and other auxiliary surgical procedures have been added. The first operation in the modern sense was performed by Friedrich[7] at Brauer's suggestion just thirty years ago (1907). Today modifications of that operation are effectively restoring to normal activities untold thousands who could not be benefited in any other way. Not only are they being saved from death and being restored to their usual occupations but they are no longer menaces to their families and associates because they no longer expectorate sputum loaded with tubercle bacilli. In the extensive review of the reported cases made by Alexander[8] in 1925 he found that approximately two-thirds of properly selected patients with chronic tuberculosis who were treated by modern surgical methods were regarded as either cured or greatly improved. The mortality rate within the first few weeks of the operation was 13.5 per cent. Today the percentage of successful results has undoubtedly greatly increased and the mortality from causes that might be ascribed to the operation has fallen to well under 10 per cent. In the best risk patients the operative mortality, even of thoracoplasty, has been reduced to the neighborhood of 1 or 2 per cent. If we could point to no other accomplishments of thoracic surgery than its enormous value in this universal scourge, we could still be proud of what it has done.

It has been noted that in the very successful attack on pulmonary tuberculosis the operations have been of a kind which do not imply the resection of any of the diseased lung tissue but that on the contrary they are for the most part performed outside of the pleural cavity. In principle, therefore, they have veered away from the pioneer operations of Tuffier and Lowson in which portions of the lung were removed. For the condition of bronchiectasis, however, the more recent surgical developments have gone back to the early principles after a lapse of many years during which the more radical principle of removing the diseased tissue was discarded. From the time of the early animal experiments of Glück,[9] Block,[10] Biondi,[11] and others, in 1881 and 1882, the thought has been present that in cases of bronchiectasis the ideal treatment would be resection of the diseased portions of the lung if the operation could be made reasonably safe. But the early operations for this condition on the human were disheartening because of the high mortality. However, as has been so often the case in the development of a new surgical procedure, one of the reasons for the excessive mortality was that only the most desperately ill patients consented to the performance of the operation. Heidenhain[12] is usually credited with the first successful lobectomy in 1901. Lilienthal's[13] impressive series of 34 cases was completed before

1925, but there was an associated operative mortality of 61 per cent. Others who undertook these operations also had high mortalities. My own first lobectomy in 1921 was followed by a thoroughly satisfactory result, but the next two died. It was but natural, therefore, that attempts should be made to devise other methods of treatment which would permit a reduction of the mortality. Various substitutes for lobectomy were tried. The procedures which had been found effective in the collapse of tuberculous cavities were tried, but, on the whole, they proved unsatisfactory. It became more and more realized that an adequate treatment of bronchiectasis must be one in which the diseased portion of lung is either removed or destroyed. All other procedures are in a sense only palliative. In 1923[14] the writer published a method whereby the adherent diseased lobe could be destroyed gradually with an actual cautery with less mortality than was prevalent at the time from lobectomy. For various reasons the method proved unsatisfactory in cases of advanced cylindrical bronchiectasis. There are patients, however, whose main lesion is multiple chronic abscesses, albeit associated with bronchiectasis in the region, who seem to be favorable subjects for this operation. In such cases lobectomy has been found to be very dangerous and simple external drainage is usually ineffective. Unless the diseased region is eradicated, the life expectancy is usually not more than two or three years. In 54 cases of that sort in which I have performed the operation 36 patients, or 67 per cent, have been able to return to their normal activities. Six, or 11 per cent, have died from the operation. Of the remaining 12 patients, 2 were moderately improved; 3, slightly improved; and 7, not improved. The encouraging fact remains that two-thirds of the patients, who represent a hopeless class of invalids, were sufficiently restored to health to go back to their regular work.

In 1929 Brunn[15] revived interest in the operation of lobectomy by reporting before the American Association for Thoracic Surgery 6 cases, with 4 cures, 1 improvement, and 1 death. In the few years which have elapsed since then the operation has found such vogue that in several hundred cases it has now been performed. An operative mortality of only 10 per cent or less is not unusual. In my own last 17 cases there has been only 1 death (5.8 per cent mortality). At the last meeting of the American Association for Thoracic Surgery, Churchill[16] was able to report a series of 49 cases with 6 per cent mortality but no mortality at all in his last 30 cases; and O'Brien[17] at the same meeting reported a series of 15 cases with 1 death. These results indicate in a most striking manner the progress which has been made, and they demonstrate that the operation in experienced hands is a thoroughly feasible procedure. Moreover, it has been learned that the most suitable cases for the operation are those of cylindrical bronchiectasis in children who at the time are free from evidence of acute pneumonitis. After the age of thirty-five or forty years, the operation becomes distinctly hazardous. The presence

of bilateral disease, however, is not necessarily a contraindication. Several instances of bilateral lobectomy (in more than one stage) have now been recorded, of which Shenstone's was the first. An obvious lesson to be derived from all of this is that children who are afflicted with cylindrical bronchiectasis, especially if it is confined to one lower lobe, should have an operation for lobectomy before the effects of chronic intoxication from the disease will make the operation too hazardous and before the child will develop the unfavorable psychological reactions resulting from more or less social ostracism and lack of attendance at school.

The next subject which I should like to discuss with you is that of primary carcinoma of the lung and I should like to discuss it more extensively than some of the other subjects because of its great importance. Since Paget's day we have learned that instead of its being a rare condition it is actually a very common one. Different compilations of statistics would indicate that this condition constitutes from 5 to 10 per cent of all cancers. That of Junghanns,[18] for example, shows in statistics from various parts of the world that this type of carcinoma represents from 2.6 to as high as 19.3 per cent of all carcinomas. We have learned also that practically all, if not all, primary carcinomas of the lung arise in the bronchial epithelium. Fried[19] locates their origin precisely in the basal layer of the bronchial epithelium, and Tuttle and Womack[20] from a study of 60 of our cases agree with his conclusions. The varied cellular morphology which one sees in these tumors (squamous cells, adenocarcinomas, "oat" cells, etc.) is all to be explained by a transformation of the basal cell into one of the various types of cells of which different tumors and even different parts of the same tumor are composed.

The frequency of bronchiogenic carcinoma is sufficiently great to make us all alert to its recognition. Yet it is disheartening to find, at least from our experience at St. Louis, that in the great majority of cases the physicians who have first seen the patients have not even considered as a possibility the true nature of the disturbance. Let us examine briefly, therefore, some of the most important diagnostic criteria. In our own cases the most common complaints have been in the following order: cough, chest pain or discomfort, dyspnea, sputum, hemoptysis or streaking of the sputum with blood, and "chest colds." A tumor which arises in a bronchus is likely to induce not only coughing and the expectoration of blood; but it is easily understood how, if it is large enough, it will cause an obstruction of the bronchus, and following that an atelectasis of the corresponding lobe. It is the atelectasis which is probably chiefly responsible for the discomfort or pain in the chest and the dyspnea. Again, as a consequence of the bronchial obstruction, various complications occur, notably bronchiectasis distal to the obstruction and infection of the lung with resulting abscess formation and sometimes even em-

pyema. The obstruction caused by the tumor is not, however, necessarily permanent at first. Variations in the amount of infection and edema of the tumor will produce changes in its size and consequently variations at different times in the amount of atelectasis which it causes. It is astonishing how often in the literature there appear reports of alleged improvements in bronchiogenic carcinoma treated by the x-ray which are based really on the erroneous assumption that the region of atelectasis observed is a true image of the tumor itself and on the assumption that because of a diminution of the shadow which is really that of the atelectatic portion of the lung the tumor is showing a marked retrogression. The region of atelectasis will sometimes clear spontaneously to a marked degree because of the variations in the swelling of the tumor already mentioned. Actually in most cases the tumor itself will not be recognizable in an x-ray examination. Despite this fact, however, the x-ray examination is of the utmost value in the diagnosis. Any patient beyond middle age who presents evidence of an atelectasis and who is known not to be tuberculous should be suspected of having bronchiogenic carcinoma. Especially is this true if the patient is a man. Moreover, he need not be of middle age, for in many instances carcinomas in this region have developed in patients between twenty and thirty years of age. If, in addition to the evidence of an atelectasis on the x-ray film, an instillation of lipiodol reveals a definite block of the bronchus, the suspicion of carcinoma will be greater.

The most important factor in the diagnosis, however, is the bronchoscopic examination. In approximately 75 per cent of cases it is possible for the bronchoscopist to see the tumor and to remove a portion of it for biopsy. In those cases, however, in which it has arisen in one of the smaller bronchi, it may be impossible to visualize it directly. It becomes evident from this brief discussion of the diagnostic features that in approximately three cases out of four it is possible to make a positive diagnosis of the condition, apart from mere conjecture or suspicion. If one includes the late cases in which evidence of marked extension or metastasis exists and in which a biopsy of the metastatic lesion or an examination of pleural fluid or of the lung itself by thoracotomy is made, an accurate diagnosis is possible during life in nearly every instance.

From the patient's standpoint the question of the treatment and of the prognosis is of more interest than the diagnosis. If a particular patient should read the literature which has accumulated on this subject during the last ten years he would doubtless gain the impression that he would have a fairly good chance of recovery with x-ray therapy, removal of the tumor by a snare through a bronchoscope or even with diathermy. There are many optimistic articles which give that impression. Especially enthusiastic have been the roentgenologists, some of whom have reported impressive series of patients apparently well three or more years after x-ray therapy. There are certain difficulties, however, about

accepting these reports. In many of the cases no biopsy was taken, and even in many in which a diagnosis of carcinoma was made by a microscopic examination no description of the microscopic appearance of the tissue is given. It happens that benign lesions of the bronchi, sometimes mistaken for carcinoma by inexperienced pathologists, are not uncommon. There can be little doubt, therefore, that many of the cases reported as carcinoma have actually been examples of benign conditions, and the enthusiasm expressed about the effects of the x-ray therapy has therefore been unwarranted. As an example of what I have in mind, let me cite the praiseworthy work of Manges,[21] of Philadelphia. In 1932 he published a series of 27 cases of supposedly positively diagnosed carcinoma subjected to treatment by roentgen therapy. At that time he thought that in 5 cases he had very gratifying results in that 2 patients were living more than nine years later; 1, six years; and the 2 others, more than three years. However, the biopsy specimens were submitted to another pathologic examination later, and in a second article[22] published after the reexamination he candidly states that all of the 5 patients just mentioned were found to have benign lesions. Of those cases which at the reexamination of the slides were still considered to be malignant the longest duration of life was only four years and most of the others were for much shorter periods. In other words, in spite of the optimism for x-ray therapy which one might gain from reading his first article, no optimism could be gained from the second one. Even the patient who lived for four years does not offer grounds for enthusiasm, for many patients with this disease live that long or even longer without any treatment. Chevalier L. Jackson,[23] also, more recently has published a paper stating that a diagnosis of a benign lesion had been made in a reexamination of the material which his father and he had collected in certain cases regarded at the time as malignant and remaining well for many years. Thus one is forced to be somewhat skeptical about many of the cases in the literature reported as having been arrested by x-ray or other minor forms of therapy. If the tumor is at all advanced, there is no satisfactory evidence that radiation therapy is of any avail, at least in the manner in which it is ordinarily used. In 19 of our patients who were treated by Dr. Sherwood Moore and his staff of the Mallinckrodt Institute of Radiology with thoroughly modern Roentgen ray equipment, not the slightest beneficial effect could be observed. Nevertheless mention should be made of certain exceptional cases. Tudor Edwards[24] states that in many cases it is possible to effect a disappearance of the growth in the bronchus by the use of radium and that in one case there was a period of three years of freedom from recurrence (up to the time of reporting). Unfortunately, however, he neglects to give us a satisfactory description of the microscopic appearance of the tumors in those cases, and he admits that in the majority of his cases the use of radium has been ineffective.

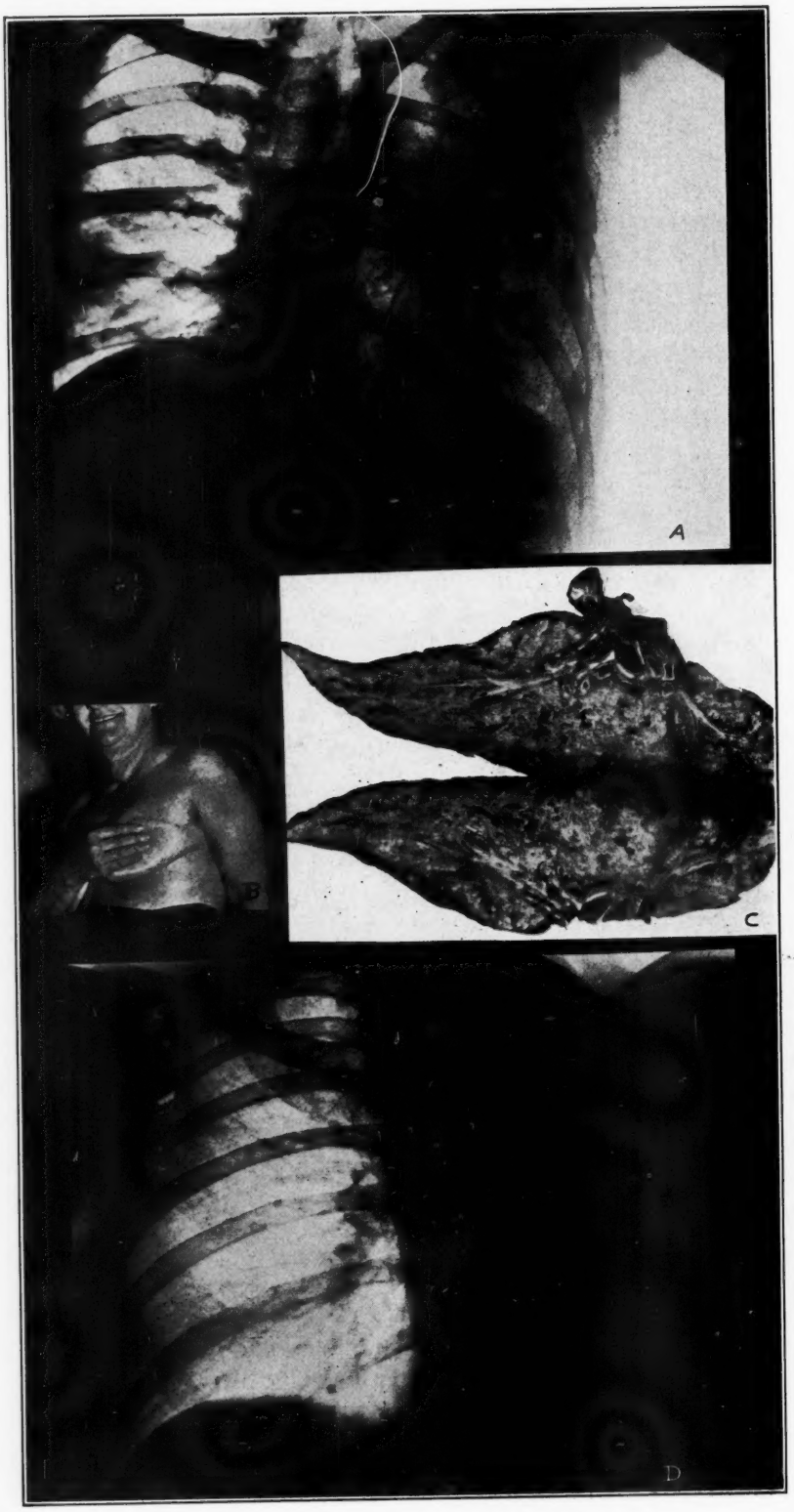


Fig. 1.—See opposite page for legend.

C. I. Allen[25] has reported a case in which, following a lobectomy for carcinoma, a persistence or recurrence of the tumor was made to disappear on four occasions during an interval of four years by the direct application of radon into the tumor. Again I have had an experience of a somewhat similar sort with one patient. Because of a squamous cell carcinoma of the lower lobe bronchus, an attempt was made to perform a total removal of the lung which, however, had to be abandoned on account of adhesions to the great vessels which seemed to me to make the operation too dangerous. Accordingly I removed only the lower lobe, and in doing so I left a portion of the carcinoma. Through the open wound Dr. Moore directed a massive dose of x-rays right at the bronchial stump and the remaining portion of tumor completely disappeared as was noted by bronchoscopic examination. The patient died at home four months later, however, of a metastasis to the brain, but his physician wrote that there was no evidence of a return of the local tumor. Such examples as I have mentioned strongly suggest that perhaps at some time a technique may be developed which will permit us to deal effec-

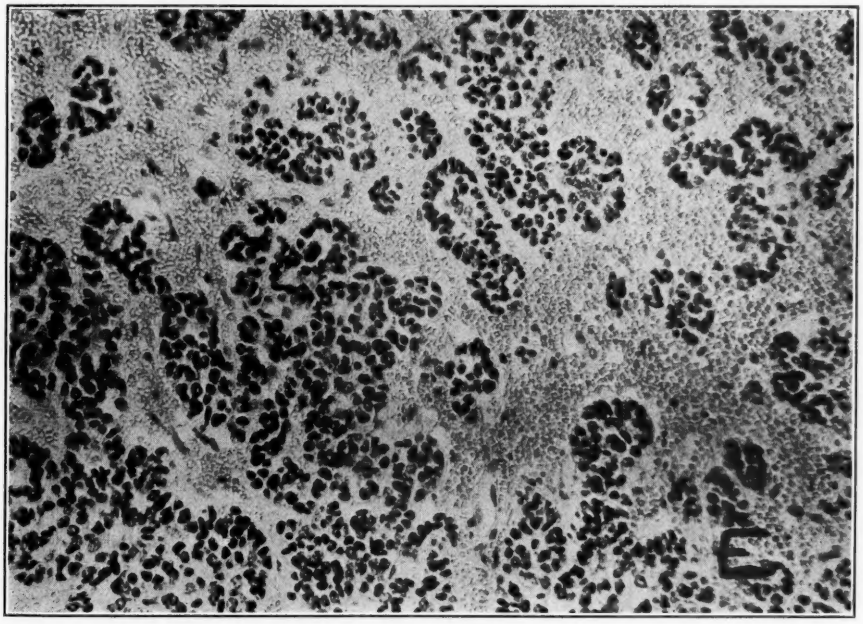


Fig. 1.—Woman, fifty years old, with carcinoma obstructing left upper bronchus. The entire left lung was removed through the incision illustrated in Fig. 5. *A*, Preoperative lipiodol x-ray film. The upper lobe bronchus is blocked by the tumor. *B*, In the photograph made six months after operation the patient is trying to show her scar to the photographer. No ribs were removed. *C*, Photograph of the removed lung after it was split open longitudinally. There is much infiltration with tumor tissue especially in the upper lobe, and the upper lobe bronchus is seen to be filled. *D*, Film made six months after operation. The right lung and mediastinal contents have moved over into the left thorax to fill the space caused by the removal of the left lung. The deviation of the trachea is plainly seen. The opacity of the left thorax is due partly to the presence of the mediastinal organs and partly to thickening of the pleura. The patient has no symptoms. *E*, Photomicrograph of microscopic structure of tumor. This is an infiltrating but slowly metastasizing carcinoma.

tively with certain early cases of bronchiogenic carcinoma by irradiation therapy, but there is no indication that such a method exists at the present time.

The most effective method at our disposal today would seem to be a radical extirpation of the tumor. Here the same surgical principles seem

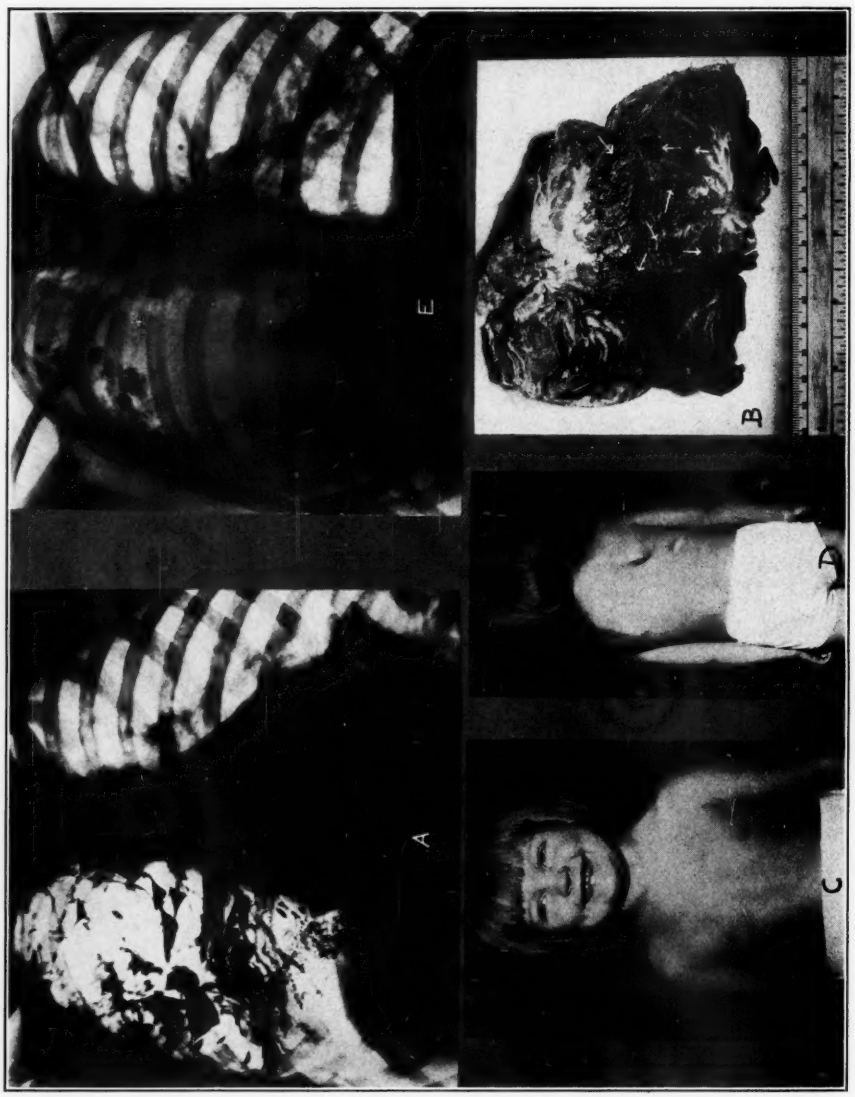


Fig. 2.—Child, four years old, with infected congenital cystic disease of right lung. *A*, In order to obtain adequate outlining of the cavities it was necessary to inject lipiodol directly into the lung through the chest wall. *B*, Photograph of the removed right lung after it was split open. Numerous cysts are evident. *C* and *D*, Photographs of the patient nine months after operation. The posterior scar represents the site of a drainage by means of a catheter inserted through an intercostal space. *E*, X-ray film nine months after operation. The reasons for the opacity of the right chest are the same as those mentioned under Fig. 1. The lipiodol shadows in the upper part of the thorax are caused by a slight residual amount of lipiodol in the chest wall following an infiltration at the time of the injection.

to be applicable as elsewhere in dealing with cancer. The removal of the whole organ involved seems more likely to be effective than the removal of only a part of it. It is not surprising, therefore, that the operation of lobectomy in general has been unsatisfactory. The patient of Allen's was living, at the last report, four years after a lobectomy, but there had been frequent recurrences in the bronchial stump which were treated with radium. So far as I know that patient has had a longer duration of life than any other patient recorded. On the other hand the total

Fig. 3.—Child, eight years old, with total bronchiectasis of left lung following the aspiration of a peanut four years previously. *A*, Shows involvement of upper as well as lower lobe. *B*, Drawing of removed left lung showing both external aspect and cut section. *C*, X-ray film eighteen months after total pneumonectomy. *D*, Photograph of patient eighteen months after operation. After the mammary gland has developed, the scar will be practically invisible.

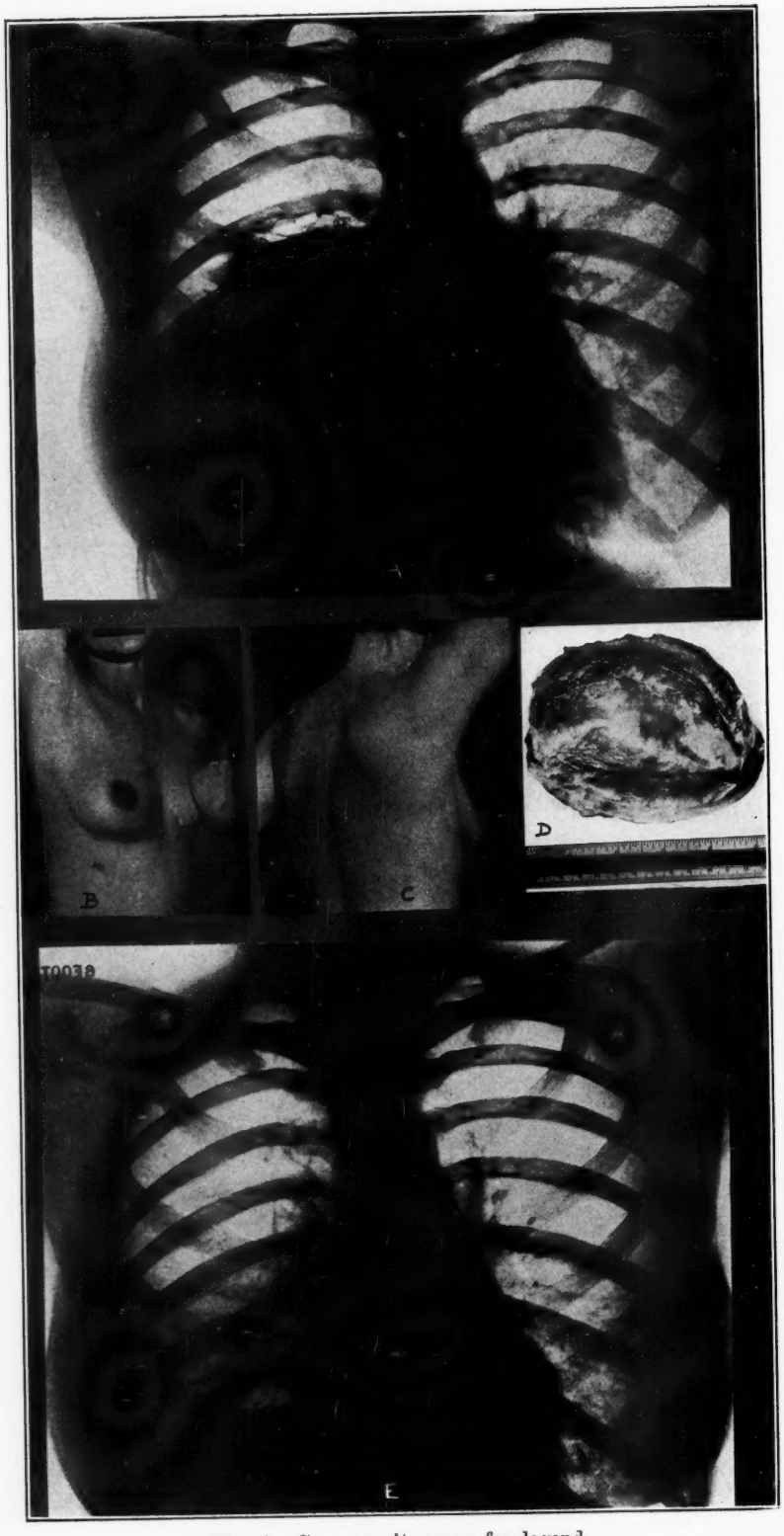


Fig. 4.—See opposite page for legend.

removal of the lung not only offers a better opportunity to get rid of all the involved lung tissue itself, but it also provides the additional advantage of being able in many instances to remove all of the pulmonary lymphatics and even many of the mediastinal lymph glands. Unfortunately it is impossible to present an imposing array of statistics on this matter at this time. The whole question of total pneumonectomy is too recent to permit that. The operation in my first case, which happened to be the first total pneumonectomy for carcinoma and incidentally the first successful total removal of the lung in one stage, was performed on April 7, 1933.[26] Although the patient is still entirely well and free from any evidence of recurrence or metastasis almost four years after his operation, it is perhaps still too short a time to feel that a permanent cure has occurred. The result nevertheless is distinctly encouraging. In another case of mine in which a total removal of the lung was performed for carcinoma the patient is alive and well almost a year after the operation. It is difficult to know with certainty in how many cases the operation has been performed successfully (that is, with survival of the patient). Survivals after operation have been reported, however, by Rienhoff,[27] Overholt,[28] Flick,[29] and Archibald.[30] It would probably be a conservative estimate to state that, in all, twelve or fifteen patients have survived the operation of total pneumonectomy for carcinoma. Many more patients will be operated upon successfully after certain technical problems have been solved and after the medical profession has been educated up to the necessity of sending the patients for operation before the disease is too far advanced. It would seem, for reasons already advanced, that the total removal of the lung is now a feasible procedure in cases of bronchiogenic carcinoma and that the operation probably offers more hope to victims of that disease than any other method of treatment now available, although it would scarcely have been thought possible a decade ago. So rapid is the progress that is being made in the field of thoracic surgery. (Fig. 1.)

The employment of the operation of total pneumonectomy, however, is not confined to cases of tumor. The operation is now finding an even wider field of usefulness in cases of cystic disease or congenital bronchiectasis or even of acquired bronchiectasis involving a whole lung. In this condition many more successful results have been obtained, and the number is rapidly increasing. In addition to three successful cases of my own in children, I know of about fifteen more in which the operation has been performed by a variety of surgeons. (Figs. 2 and 3.) A good review of the literature of cases of total pneumonectomy reported up to

---

Fig. 4.—Large dermoid cyst of anterior mediastinum. *A*, In the x-ray film the tumor is seen projecting over to the right side. *B* and *C*, are photographs made at the time of the discharge of the patient from the hospital, four weeks after the operation. Two years later the scar was practically invisible. The small scar below the line of incision marks the site of a closed intercostal drainage to allow the collected fluid to escape from the pleural cavity. *D*, In the photograph of the specimen it will be seen that the long diameter of the cyst is more than 13 cm. *E*, This x-ray film made six months after the patient's discharge shows how impossible it would be to detect that the patient had ever had an intrathoracic operation because of the complete absence of any deformity.

1934 is given by Haight[31] who was the first in this country to remove an entire lung for bronchiectasis by allowing the lung to slough out after ligating the hilus.

Before closing this brief and rather superficial review of the accomplishments of thoracic surgery in the last forty years, it would be unfortunate not to mention two other conditions in which a marked advance has been made. I refer on the one hand to mediastinal tumors and on the other hand to the heart. In Paget's day about the only treatment applicable to tumors of the mediastinum was the drainage of those which were cystic. Now we realize that, if we exclude aneurysms and substernal adenomas of the thyroid, the tumors of the anterior mediastinum are in general of two kinds. One of these is that group which comprises those tumors which arise in the lymph glands or the thymus. Such tumors as a rule are malignant but they undergo marked temporary retrogression with x-ray therapy. In our opinion surgical treatment is not indicated in those cases. The other group comprises a number of tumors arising from different elements. In this group one may find almost any of the ordinary benign tumors, but of particular importance are those which seem to arise definitely in misplaced fetal remnants, such as the dermoids and teratomas. It is not generally realized that thoracic dermoids and teratomas arise almost exclusively in the anterior mediastinum. The tumors of this group are radioresistant, and they should be removed by a surgical operation unless other features of the patient's condition contraindicate their removal. It is especially important to remove teratomas because of the great danger of their becoming malignant. Tumors of the posterior mediastinum as a rule are derived from nerve or bone elements. They are seldom affected by x-ray therapy. Our usual procedure in handling a tumor of the mediastinum is to subject it first to a course of x-ray therapy. If it shows a distinct diminution after such treatment, no operation is performed. If, on the other hand, it is not affected by irradiation, operative removal is performed. Again, it is astonishing to those who have not kept abreast of the progress in thoracic surgery that such tumors, even large ones, can now be removed with a mortality of only approximately 10 per cent or less and moreover in such a way that there is no deformity of the chest. Out of a total experience of 45 mediastinal tumors, exclusive of aneurysms and substernal thyroids, we have been able to remove 9 with 1 death which occurred three weeks after operation from an infection of the mediastinum. Five of these were dermoids. I have purposely omitted from the discussion those examples of mediastinal tumor which represent metastatic involvement of the mediastinal glands with carcinoma from elsewhere in the body. They belong to a different category and present no indication for surgical interference. (Fig. 4.)

As regards the heart, mention has already been made of the great improvement in mortality effected in penetrating wounds of that organ. For a number of years attempts by surgical methods have been made to

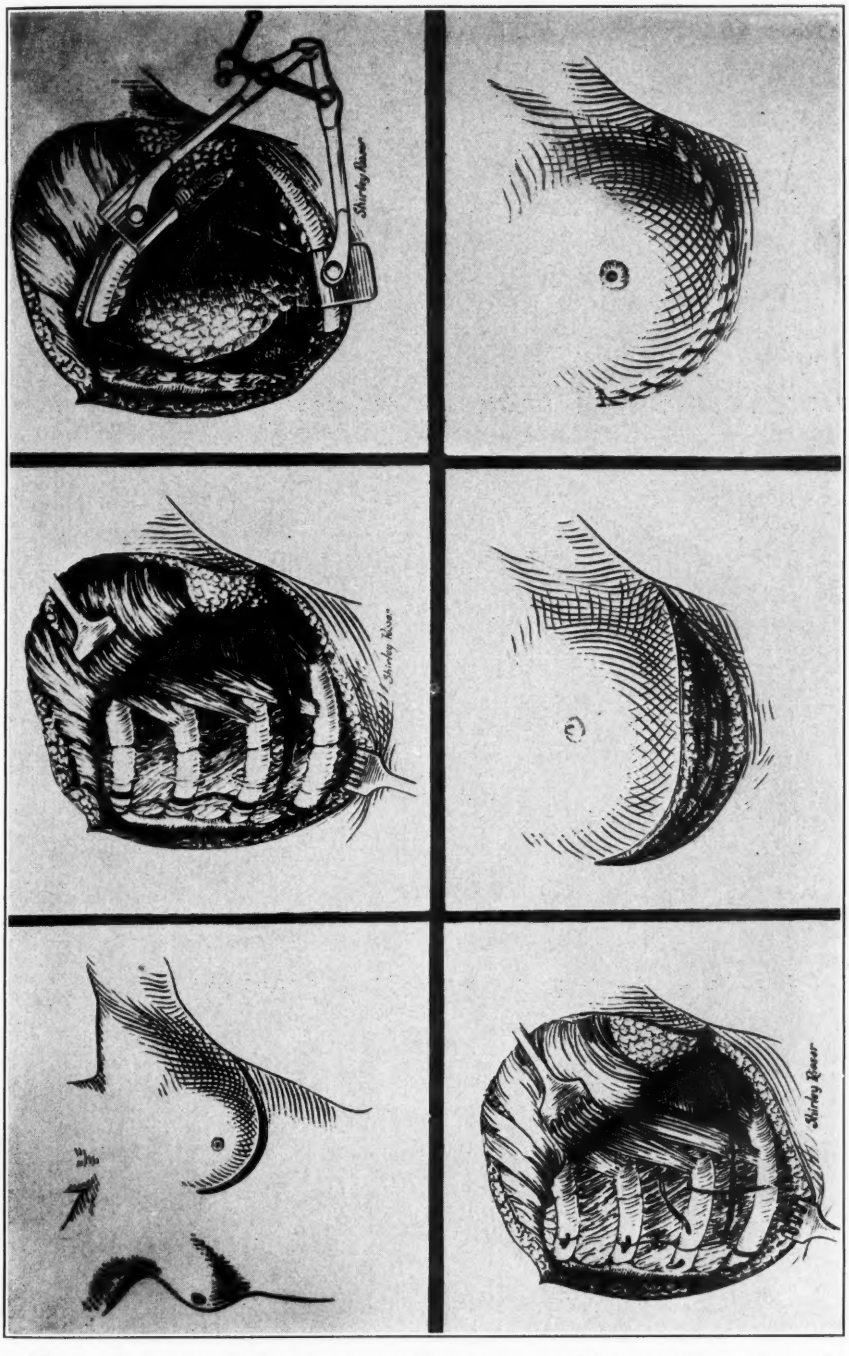


Fig. 5.—By means of this submammary incision an excellent cosmetic result can be obtained after the removal of many mediastinal tumors and even a whole lung. The breast and pectoralis major muscle are dissected upwards. Several costal cartilages are divided and an intercostal incision is made. The divided ends of the cartilages are sewn together with a cutting needle and No. 2 chromic catgut. Another suture of No. 2 catgut is placed around the two lowest ribs concerned. The cosmetic result is so good in women that after a year or two it is impossible to detect that they have undergone an operation. Even an x-ray photograph will fail to reveal any evidence of the operation. Somewhat similar incisions have been used by Rienhoff and Overholt.

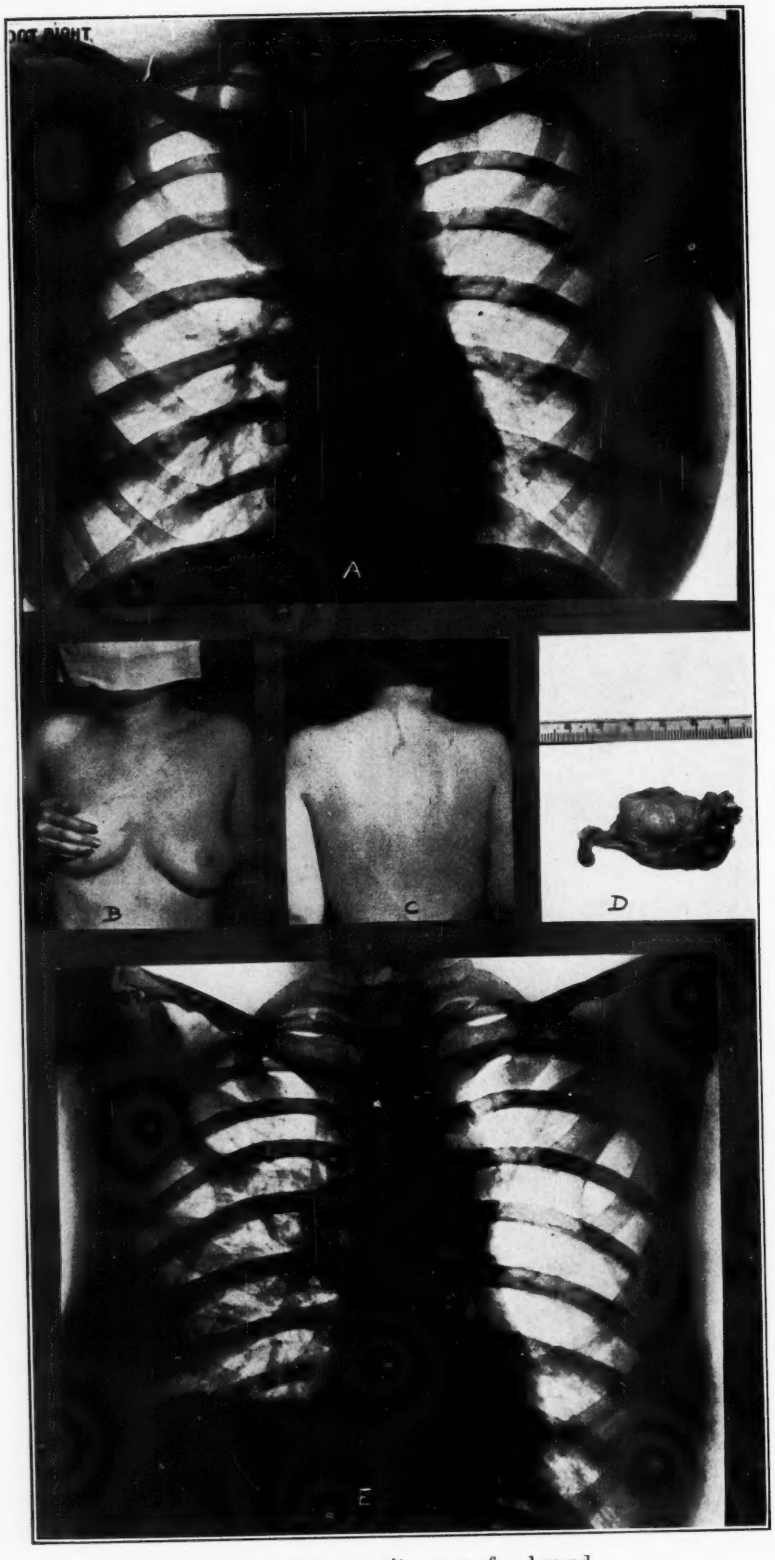


Fig. 6.—See opposite page for legend.

relieve the symptoms, if not actually to improve the condition of the heart itself, in angina pectoris. The operations on the sympathetic nervous system, although at first encouraging, have proved to be of so little permanent value that apparently in recent years they have been largely abandoned. The same can be said for the more recent operation of total thyroidectomy for this condition. During the last two or three years, however, Claude Beck[32] and his colleagues have attacked the problem with a new principle which is brilliant in conception and which seems to have accomplished very encouraging results in some of the patients to whom it has been applied. It seems to me probable that in selected cases Beck's operation will be found to be far more satisfactory than any other known method of handling these distressing cases. From the known evidence that in such cases the fundamental trouble is an ischemia of the myocardium from partial occlusion or spasm of the coronary arteries, Beck undertook to improve the circulation of the heart muscle by a more direct method than had hitherto been employed. He found in carefully conducted experiments on animals with coronary occlusion that new blood vessels would grow into the myocardium if a flap of healthy muscle were approximated to the heart. His operation then consists of applying part of the pectoralis major muscle directly to the myocardium in cases of angina pectoris. The operation is well tolerated despite the serious condition of the heart and some of his patients who were formerly completely incapacitated are now able to do heavy manual labor. If the condition of angina pectoris becomes amenable to successful surgical treatment, the lives of many thousands of sufferers will be made happier.

Another accomplishment in recent years has been the improvement in technique which has made it possible to perform even extensive thoracic operations without an appreciable deformity of the patient. A decade ago many patients, and their physicians too, shuddered at the thought of an operation on the chest because in their minds it entailed an inevitable horrible deformity even if the patient should survive. Much of this fear can now be dispelled. Even extensive intrathoracic operations can now be performed, especially on women who are perhaps most concerned, without any visible evidence, either externally or on subsequent x-ray examination, that any operation has been done. The proof of this statement will be shown you on some lantern slides. This accomplishment in itself seems to me a triumph. (Figs. 5 and 6.)

In this brief survey of what has been done in thoracic surgery since Paget's pessimistic prophecy only some of the accomplishments have been discussed. It would be impossible in a single lecture to mention, however briefly, all of them. I am sorry that I have not been able to speak of the

Fig. 6.—Patient, nineteen years old with multilocular cyst (probably cystic hygroma) in upper anterior mediastinum. *A*, The x-ray film shows the high location of the tumor. *B* and *C*, In spite of its high location it was possible to remove the tumor through the anterior submammary incision with an excellent cosmetic result as shown in the photographs taken at the time of the patient's discharge. *D*, The removed tumor is seen in the photograph to measure 5 cm. in length. *E*, The x-ray film made four weeks after operation shows a complete absence of deformity.

many interesting facts in the fields of physiology and pathology which have been learned as a result of operating within what was formerly the forbidden territory of the thorax. I am likewise sorry that it has been impossible to mention more than a very few names of that rapidly increasing group who are making important contributions to this field. We in the United States were somewhat slower than our European colleagues to undertake thoracic surgery on a major scale; but now, having entered it, we have perhaps forged ahead of them in the speed of our development of new techniques and in our broadening of the indications of this form of therapy. We can boast of a very active society devoted exclusively to this field, the American Association for Thoracic Surgery, which is twenty years old this year, and to a successful *Journal of Thoracic Surgery* which is now in its sixth year.

Of the problems which face us, again I can mention only a few. The esophagus is an organ which in the main has still withstood our assaults. The proper principle for the successful treatment of carcinoma of that organ, in my opinion, is yet to be developed. Since the carcinomas of this organ are of a squamous cell variety and thus resemble those of the mouth and of the cervix uteri, it seems strange that the good results of radiation therapy for carcinoma of the latter organs have not been duplicated in the esophagus. Probably the reason is that the irradiation has not been given in the most effective way. As regards carcinoma of the bronchus, several problems face us acutely. One of these is better pathologic diagnosis. Until we can be more certain than it is possible to be today, without at least published photomicrographs of the tumor, we can have no reliance on reports of cases said to be cured by this or that method. The general profession needs to be educated and aroused to the fact that this is a common disease, of the same order of frequency as carcinoma of the colon including the rectum, and that suspicious cases should be subjected early to x-ray and bronchoscopic examination. Less than 5 per cent of the cases which we see at St. Louis can be considered as suitable for operation. In this connection a word should be said about prognosis. In our experience, based on the study of our cases by Tuttle and Womack,[20] the prognosis is better both for duration of life and for operability in those cases in which the tumor has arisen in one of the major bronchi than in those in which it has arisen near the periphery of the lung in one of the smaller bronchi. Rabin and Neuhof,[33] however, hold the opposite opinion. This is a matter of considerable importance and one which perhaps demands still more work on it. When some of these matters are settled more definitely perhaps we can then determine more accurately whether surgery, irradiation or some other form of therapy is the most suitable and most effective procedure in this dread disease. Finally may I mention that another major problem is to find a more effective control of the necrotizing and putrid types of infection which commonly occur in the lung and which often baffle our best surgical efforts.

REFERENCES

1. Paget, Stephen: Surgery of the Chest, Bristol, 1896, John Wright & Co., p. 207.
2. Roberts: Quoted by Paget, p. 372.
3. Elkin, D. C.: Wounds of the Heart: Report of Thirteen Cases, J. Thoracic Surg. **5**: 590, 1935-36.
4. Graham, E. A., and Bell, R. D.: Open Pneumothorax: Its Relation to the Treatment of Empyema, Am. J. M. Sc. **156**: 839, 1918.
5. Burdon, K. L.: Bacterium Melaninogenicum From Normal and Pathological Tissues, J. Infect. Dis. **42**: 161, 1928.
6. Varney, P. L.: Bacterial Flora of Treated and Untreated Lung Abscess, Arch. Surg. **19**: 1602, 1929.
7. Friedrich, P. L.: Die Operative Beeinflussung einseitiger Lungenphthise durch totale Brustwandmobilisirung und Lungenentspannung (Pleuro-Pneumolysis totalis), Verhandl. d. deutsch. Gesellsch. f. chir., **37**: 534, 1908; also, The Operative Treatment of Unilateral Lung Tuberculosis by Total Mobilization of Chest Wall by Means of Thoracoplastic Pleuro-Pneumolysis, Surg., Gynec. & Obst. **7**: 632, 1908.
8. Alexander, John: The Surgery of Pulmonary Tuberculosis, Philadelphia, 1925, Lea & Febiger.
9. Glück: Quoted by Paget.
10. Block: Quoted by Paget.
11. Biondi: Quoted by Paget.
12. Heidenhain, L.: Ausgedehnte Lungenresection wegen Zahlreicher eiternder Bronchiectasien in einem Unterlappen, Verhandl. d. deutsch. Gesellsch. f. Chir. **30**: 636, 1901.
13. Lilienthal, H.: Thoracic Surgery, Philadelphia, 1925, W. B. Saunders Company, vol. II, p. 216.
14. Graham, E. A.: Pneumectomy With Cautery, J. A. M. A. **81**: 1010, 1923; also Cautery Pneumonectomy for Chronic Suppuration of Lung, Arch. Surg. **10**: 392, 1925.
15. Brunn, H., Surgical Principles Underlying One-Stage Lobectomy, Arch. Surg., **18**: 490, 1929.
16. Churchill, E. D.: To be published in J. Thoracic Surg.
17. O'Brien, E. J.: To be published in J. Thor. Surg.
18. Junghanns, H.: Der Krebs der Lungen, Bronchien und oberen Luftweg, Ztschr. f. Krebsforsch. **28**: 573, 1928.
19. Fried, B. M.: Primary Carcinoma of the Lung, Medicine **10**: 373, 1931.
20. Tuttle, W., and Womack, N. A.: Bronchiogenic Carcinoma; A Classification in Relation to Treatment and Prognosis, J. Thor. Surg. **4**: 125, 1934.
21. Manges, W. F.: Primary Carcinoma of the Lung: Roentgen Diagnosis and Preliminary Report on Roentgen Therapy, Am. J. Roentgenol. **27**: 858, 1932.
22. Manges, W. F.: An Analysis of a Group of Primary Newgrowths of the Lungs Treated With Deep X-ray Therapy, Radiology **22**: 423, 1934.
23. Jackson, C. L., and Konzelman, F. W.: Bronchoscopic Aspects of Bronchial Tumors, With Special Reference to So-called Bronchial Adenoma (Reports of Twelve Cases), J. Thoracic Surg. **6**: 312, 1937.
24. Edwards, T.: Malignant Disease of the Lung, J. Thoracic Surg. **4**: 107, 1934-35.
25. Allen, C. I.: A Case of Primary Carcinoma of the Lung. Report Four Years After Lobectomy, J. Thoracic Surg. **4**: 224, 1934.
26. Graham, E. A., and Singer, J. J.: Successful Removal of an Entire Lung for Carcinoma of the Bronchus, J. A. M. A. **101**: 1371, 1933.
27. Rienhoff, W. F., Jr.: The Surgical Technic of Total Pneumonectomy, Arch. Surg. **32**: 218, 1936.
28. Overholt, R. H.: Surgical Treatment of Carcinoma of the Lung, Surg., Gynec. & Obst. **64**: 209, 1937.
29. Flick, J. B.: Personal communication.
30. Archibald, E. W.: The Technic of Total Unilateral Pneumonectomy, Ann. Surg. **100**: 796, 1934.
31. Haight, C.: Total Removal of Left Lung for Bronchiectasis, Surg., Gynec. & Obst. **58**: 768, 1934.
32. Beck, C. S.: Further Data on the Establishment of a New Blood Supply to the Heart by Operation, J. Thoracic Surg. **5**: 604, 1936.
33. Rabin, C. B., and Neuhof, H.: A Topographic Classification of Primary Cancer of the Lung. Its Application to the Operative Indication and Treatment, J. Thoracic Surg. **4**: 147, 1935.

THE USE OF MUSCLE FLAPS IN THE CLOSURE OF CHRONIC EMPYEMA CAVITIES

B. Noland Carter, M.D., Cincinnati, Ohio

(From the Department of Surgery of the College of Medicine, University of Cincinnati, and the Cincinnati General Hospital)

MANY chronic empyema cavities will obliterate themselves completely or in part if they are provided with really adequate drainage. This fact has been stressed especially by Hedblom, Colonel William Keller, and Graham and cannot be too strongly emphasized. Particularly is this true of those cases of chronic empyema which are of relatively short duration. Generally speaking, however, there are three types of chronic empyema in which complete obliteration of the cavity does not occur even under ideal conditions of drainage. These are (1) cases of secondarily infected tuberculous empyema, (2) cases of nontuberculous empyema that have lasted several years, and (3) cases of chronic empyema complicated by bronchial fistulae. The secondarily infected tuberculous empyema presents an especially difficult problem as to healing, for the lung and pleura are usually so fibrosed that expansion of the lung is impossible, and, even if it were, one would hesitate to expand it for fear of lighting up the quiescent tuberculosis in it. In this type of chronic empyema, therefore, the surgeon must obliterate the *entire* cavity by plastic operations on the thoracic wall, since nature cannot contribute anything in the way of expansion of the lung. In cases of long standing nontuberculous empyema, also, there has been great thickening of the visceral and parietal pleura, and the lung which has been compressed for so long a time is apt to have become so fibrosed that it can never fully expand. Here, however, after adequate drainage has been established and after active Dakinization has been carried out, there is nearly always some decrease in the size of the cavity owing to the partial re-expansion of the lung. Bronchial fistulae are serious complications, owing to the fact that they interfere with lung expansion, reinfect the wound, and preclude active irrigation of the cavity. It is evident, therefore, that many cases of chronic empyema will reach a stage during their treatment when a cavity which cannot, without further surgical treatment, decrease in size is still present. It is with the management of such persistent cavities that this paper deals.

The first and most important requisite in treatment of chronic empyema is to create ideal conditions of drainage. The resection of short segments of one or two ribs and the introduction of a large rubber tube *does not* constitute adequate drainage. The chest wall should be

Received for publication, Nov. 29, 1937.

widely opened by the resection of at least four inches, and preferably of six inches, of two or three ribs situated at the lower most portion of the empyema cavity (see Fig. 4). The thickened parietal pleura thus exposed is excised to the limits of the incision laterally and to the re-

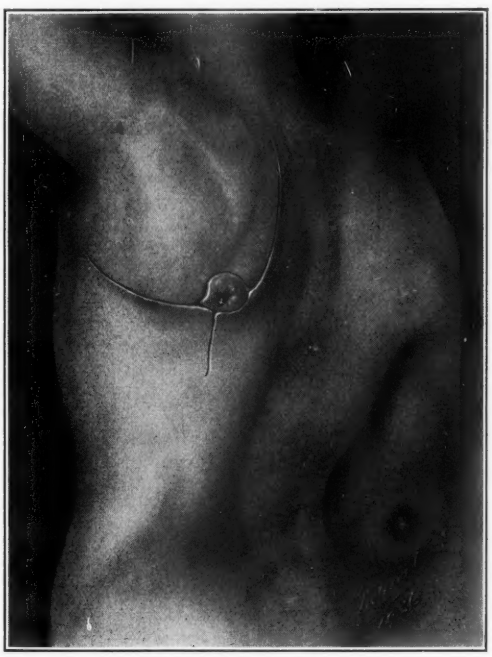


Fig. 1.—The incision. Note especially the short vertical incision; by reflecting the flaps thus formed additional muscle can be exposed and utilized.

Fig. 2.—The skin flaps below have been reflected exposing considerably more muscle than could be reached through a single incision.

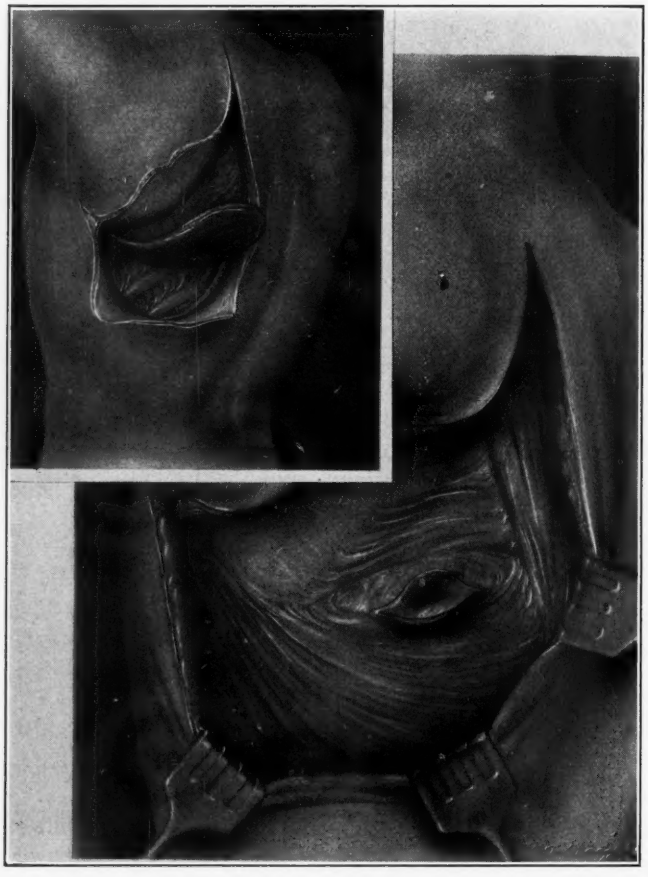


Fig. 3.—The dotted line indicates the incision through the muscles. Note the additional length of the muscle flap below the sinus tract. Insert shows muscle flap freed and raised.

Fig. 4.—Four-inch segments of two ribs have been resected and the intercostal muscle has been preserved. The thickened parietal pleura is being excised, thus creating a large opening into the empyema cavity.

maining ribs above and below. This produces an opening four to six inches long and three or four inches wide into the dependent portion of the cavity. Through such an opening the interior of the cavity can be inspected, foreign bodies removed, if present, bronchial fistulae discovered, and pockets found. Likewise, thorough irrigations with Dakin's

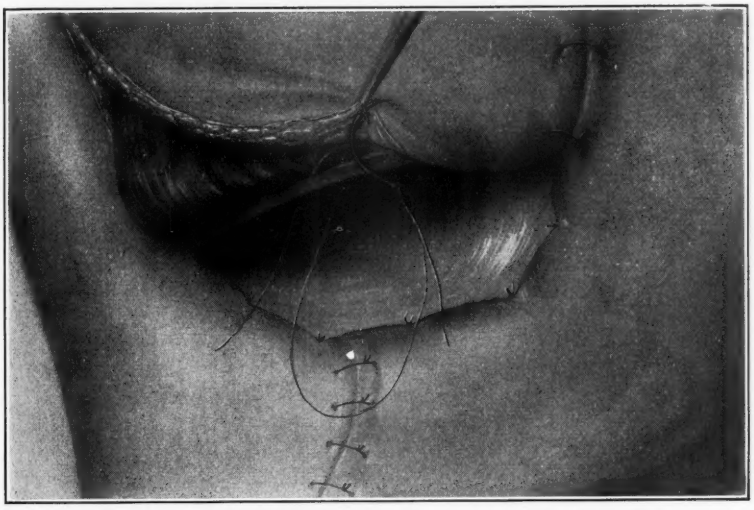


Fig. 5.—The cavity is being exteriorized by suturing the skin edges to the edges of the pleura. Note that the muscle flap has been carefully tucked under the upper skin flap which is being tacked down to the pleura.

Fig. 6.—The completed first stage. A large opening has been made into the dependent portion of the empyema cavity which provides adequate drainage and through which the cavity can be thoroughly inspected and adequately treated. No tubes are necessary, for the opening cannot close unless the lung has fully expanded.

solution or azochloramide can be carried out and light packs saturated with these solutions can be placed in contact with the walls of the entire cavity. No drainage tubes are needed, for by sewing the skin edges to the edges of the pleura the cavity is exteriorized and the opening into it cannot close (Fig. 6).

Having been thus exteriorized, the cavity should be treated with Dakin's solution or azochloramide until it has been obliterated by the gradual expansion of the lung or until it has ceased to decrease in size. If complete expansion occurs, the skin edges can be freed and readily closed; whereas, if incomplete expansion results and a residual cavity remains, a more extensive plastic operation must be done.

The procedure used to obliterate the cavity which persists after thorough drainage and active treatment with Dakin's solution or

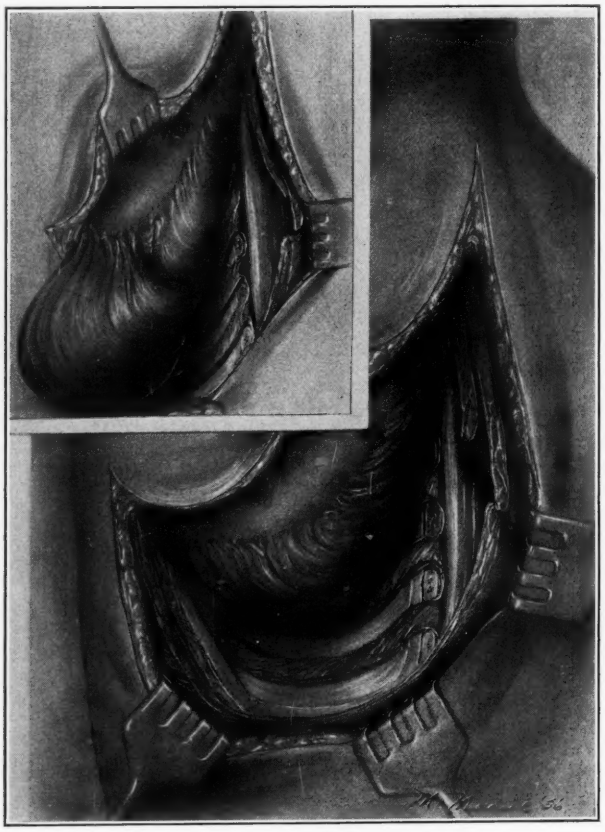


Fig. 7.—Following the first stage, there has been a persistent cavity which has ceased to decrease in size. The cavity has been Dakinized until nearly sterile and the patient's condition has improved to the extent that a second operation can be safely undertaken. Further "unroofing" has been done; the muscle flap has been mobilized and it is being tucked into the cavity beneath the scapula. The intercostal muscles are also utilized for filling the cavity.

azochloramide have accomplished all that is possible will depend upon the type, the size, and the location of such a cavity. In the case of a chronic empyema cavity with relatively thin parietal pleura, an extrapleural thoracoplasty done in many stages and with formalinization of the rib beds will close a residual cavity or greatly decrease its size. If, however, the parietal pleura is very thick, a simple thoracoplasty will not appreciably diminish the size of a cavity; for even though the ribs

be resected from spine to sternum, the rigid pleura continues to hold the cavity open. The small cavity in the lower thorax can be obliterated simply by the resection of the ribs and the thick pleura overlying it and by allowing the soft tissues to fall into and fill the cavity. However, the large cavities in the lower portion of the thorax, those cavities that lie beneath the scapula, and also those at the apex of the thoracic cage cannot be closed so easily. The scapula will not fall completely in contact with the underlying lung after the ribs beneath it have been resected,

Fig. 8.—The closure of a huge empyema cavity. After several stages, the cavity has finally been widely "unroofed." The sacrospinalis has been mobilized, divided, and is being used to fill the upper portion of the cavity. The intercostal muscles have been preserved and used to help fill the large cavity. The next drawing shows the remainder of the cavity filled with trapezius and latissimus dorsi muscles. If the cavity is not too deep, the intercostal muscles fall on to the floor of the cavity without having to be divided, thus preserving the intercostal nerves.

and, unless a "fill" of some sort is placed beneath the scapula, a dead space which may give rise to a recurrence of the empyema (Fig. 13) will persist. The configuration of the thorax at the apex is such that cavities situated there will not be filled by the falling in of the soft tissues when the ribs overlying the cavity have been removed. It is in these instances that flaps of muscles can be swung into the empyema cavity in order to obliterate it. The muscles which are available for this purpose are the latissimus dorsi, the trapezius, the sacrospinalis, and the pectorals.

Before the muscle flap is swung into a cavity situated in the lower portion of the thorax, the ribs should have been removed beyond the limits of the cavity and the parietal pleura excised to the margins of the cavity. In the case of some of the cavities that extend to the apex or under the scapula not all the ribs over the cavity need be removed, the resulting recess beneath one or two ribs being filled with the muscle flaps. The cavity should be sterile, or nearly so, before the muscle is placed in it. In the case of extensive cavities the "unroofing" by means of resection of the ribs and thickened parietal pleura must be done in several stages.

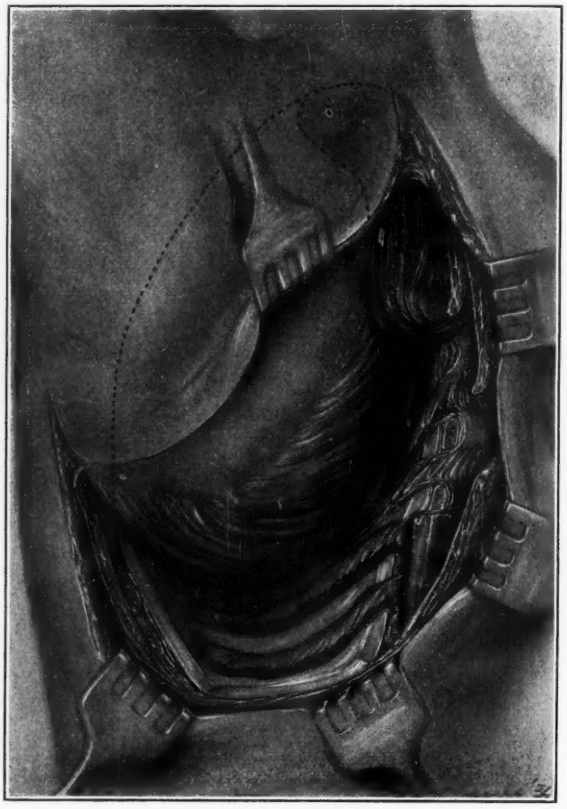


Fig. 9.—The huge persistent empyema cavity has been filled with muscle flaps—the apical portion with a flap of sacrospinalis muscle, the subscapular portion with a flap of trapezius and latissimus dorsi muscles, and the remainder partly with the above and with intercostal muscle.

Patients who have suffered from chronic empyema for years are not good surgical risks, and the resection of the large triangular ribs which have been squeezed together by contraction of the chest wall is often a bloody and difficult procedure. It is far better, therefore, to break the operation up into several stages at each of which a few ribs are resected, rather than to risk the danger of a complete unroofing at one sitting.

In order to get enough material to fill the cavity it is important that one plans the operation so as to utilize every bit of muscle possible. A

very useful method of obtaining added bulk of muscle is to make a second incision at right angles to the one which has been placed at the lower most border of the empyema cavity, to reflect the skin flaps thus formed, and to cut the muscle which is to be utilized at a considerably lower level (Figs. 1, 2, and 3). In this way several inches of muscle may be gained. The intercostal muscles should be carefully preserved when possible and likewise utilized as a "fill." They are especially useful to plug bronchial fistulae after the method of Pool and Garlock and of Shenstone. If the cavity is not too deep, they may be preserved intact (not divided as shown in the figures) and allowed to fall into the floor of the cavity. Wangensteen has advocated preserving the intercostal

Fig. 10.—Closure after the final stage. The sutures are placed very loosely. No drains are used.

muscles with the veins and vessels and using them with the strip of attached thickened parietal pleura to help fill empyema cavities. I prefer to strip the thickened pleura off the under side of the intercostal muscle and excise it rather than use it and the muscle together, for the pleura may be riddled with small sinuses leading to minute abscess cavities and if preserved these may reinfect the cavity or the wound. The presence of small abscesses and infected sinus tracts in the parietal pleura has been noted in several of my cases and has been referred to by other authors. This may well be a cause for "the recurrent chronic empyema." It is for this reason that the thick parietal pleura should be excised rather than utilized as a material with which to fill the empyema cavity.

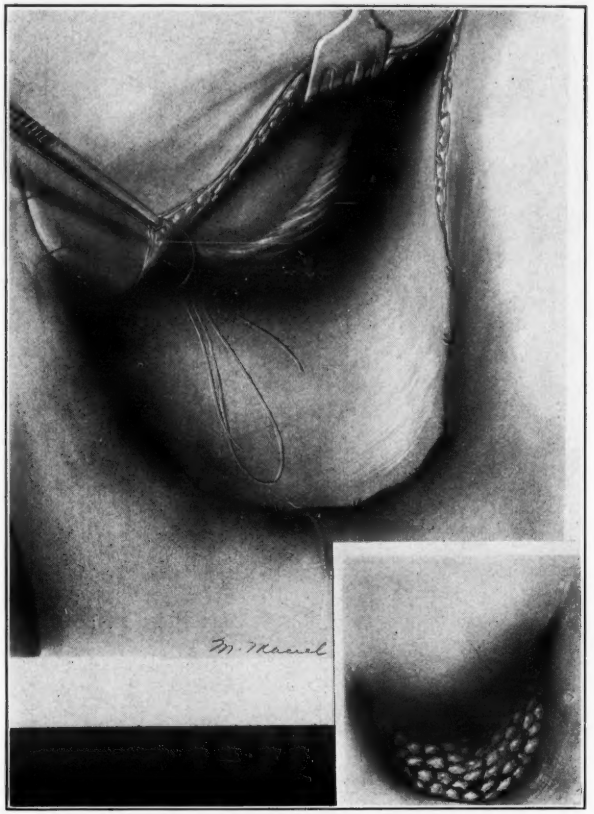


Fig. 11.

Fig. 12.

Fig. 11.—The amount of muscle available was insufficient to fill the cavity. The majority of the muscle has been used to fill the upper portion of the cavity, i.e., at apex and under scapula. The skin edge is being sewed down to the pleura, leaving a large area of pleura uncovered. The insert shows this area of pleura covered with pinch grafts.

Fig. 12.—The use of muscle flaps in the closure of bronchial fistulae. The intercostal muscles are especially useful, but, if they are not available, slips of other muscles, such as the sacrospinalis or latissimus dorsi, can be utilized.

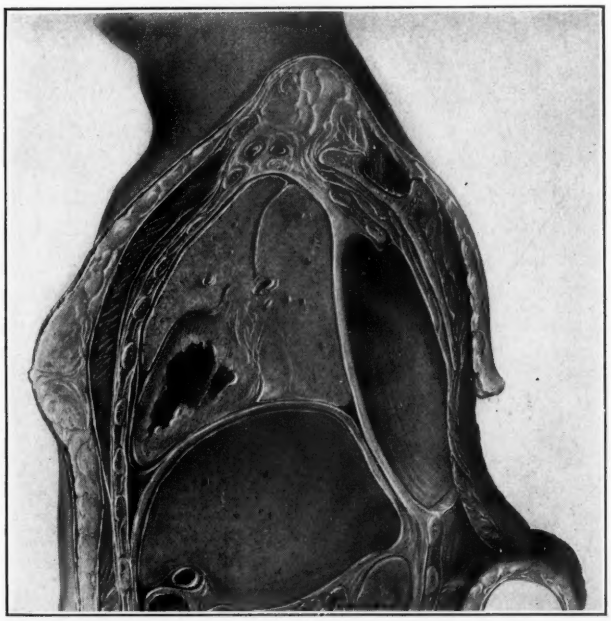


Fig. 13.—A sagittal section through the thorax to show dead space still existing beneath the scapula even after the overlying ribs and pleura have been excised. Note the long flap of muscle ready to be thrown into the cavity.

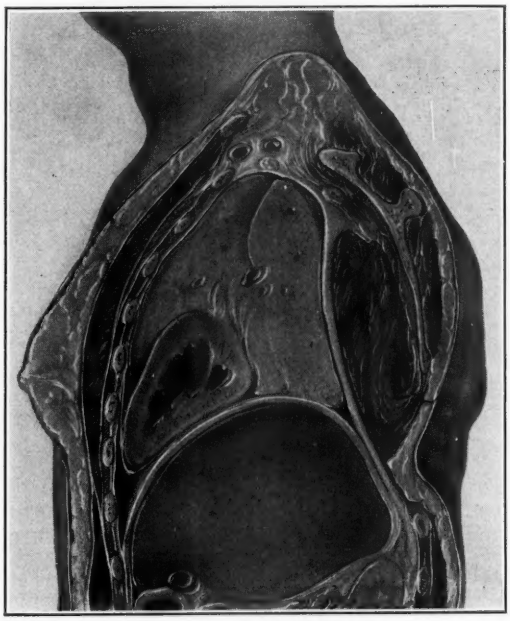


Fig. 14.—The empyema cavity and the dead space beneath the scapula have been filled with muscle flap.

Fig. 12.—The use of muscle flaps in the closure of bronchial fistulæ. The [illegible] can be utilized, if they are not available, slips of other muscles, such as the sacrospinalis or latissimus dorsi,

Another reason for its excision is that in tuberculous empyema (10 per cent to 13 per cent of chronic empyemata) the parietal pleura practically always is the site of tubercles or tuberculous granulation tissue.

The accompanying illustrations show the steps in the various operative procedures and need little explanation. Unless the empyema cavity is very large, relatively little deformity is present after the operation. The sacrospinalis muscle may be very satisfactorily utilized in filling empyema cavities at the apex and under the upper portion of the scapula. Though no illustrations are shown of them, the pectoral muscles can best be utilized for empyema cavities in the anterolateral aspects of the thorax.

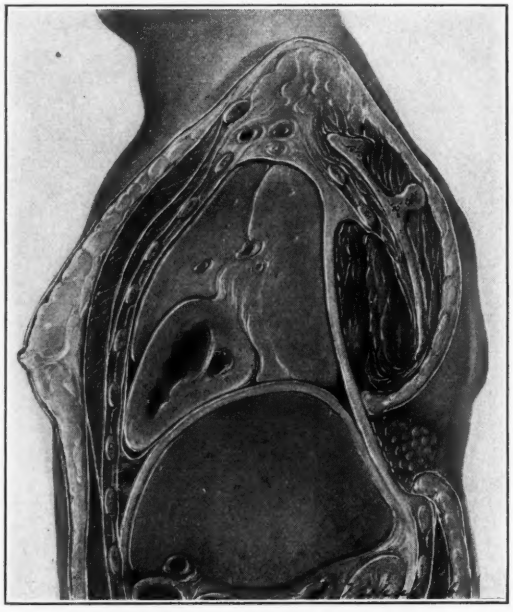


Fig. 15.—Only enough muscle to fill a portion of the cavity and the dead space beneath the scapula was available. The upper skin edge has been sewed down to the pleura, thus leaving a considerable extent of pleura exposed which has been grafted with pinch grafts (see Fig. 11).

The use of pedicled muscle flaps has been found to be very satisfactory in this clinic in dealing with the persistent chronic empyema cavity, in the closure of extrapleural cavities resulting from the excision of cold abscess of the chest wall, in the cure of chronic lung abscess, and in the secondary closure of infected thoracoplasty wounds in which an extrapleural cavity remains beneath the scapula. In the literature, however, there are relatively few references to their being used. S. Robinson, in an excellent article in 1916, described their use in the closure of nontuberculous chronic empyema. He stated that "muscle can be swung into the cavity and is an efficient filling agent" and believes that by their use such mutilating operations as the resection of a portion of the scapula over chronic empyema cavities can be dispensed with. He likewise advo-

cates partial filling of a large cavity with a muscle flap leaving the rest to epithelialize—a procedure somewhat similar to the one shown in Fig. 11. Kanavel, in 1921 in an article entitled "Plastic Procedures for Obliteration of Cavities" describes the utilization of a muscle flap in the filling of various residual cavities, such as those of chronic osteomyelitis, of chronic empyema, and of one large cavity behind the symphysis. He was very enthusiastic about its use and wondered why it was not more often used. Stenbuck in 1933 used pedicled muscle flaps to close defects in the pleura. Graham in 1924 mentioned their use in the treatment of chronic empyema. Scrimger in 1929 used flaps of the rhomboid muscle to close a lung abscess cavity at the apex, and in a discussion of his paper Whittemore reported five cases of his own, similarly treated. Pool and Garlock closed bronchial fistulae by inserting muscle flaps into them. Wangensteen in 1935 advocated the use of muscle flaps in the closure of bronchial fistula and chronic empyema. Alexander advises the use of muscle flaps in the closure of certain chronic empyema cavities in his recent monograph on *The Collapse Therapy of Pulmonary Tuberculosis.*

The purpose of this paper has been to emphasize the fact that adequate drainage by the resection of long segments of several ribs and wide exteriorization of the empyema cavity is the most important step in the treatment of chronic empyema; to call attention again to the advantage of using pedicled muscle flaps in the closure of the chronic empyema cavity that remains after adequate drainage has accomplished all it can; and to illustrate several useful technical points in obtaining and utilizing various muscles which can be used as "fills."

REFERENCES

Alexander, John: The Collapse Therapy of Pulmonary Tuberculosis, Springfield, Ill., 1937, Charles C. Thomas, p. 616.
Bettman, R. B.: Arch. Surg. **8:** 418, 1924.
Graham, E. A., Singer, J. J., and Ballon, H. C.: Surgical Diseases of the Chest, 1935, Philadelphia, Lea & Febiger, p. 154.
Graham, E. A.: Surg. Gynec. & Obst. **38:** 466, 1924.
Heuer, G. J.: Ann. Surg. **72:** 80, 1920.
Hedblom, C. A.: Ann. Surg. **72:** 288, 1920.
Kanavel, Allen B.: Surg., Gynec. & Obst. **32:** 453, 1921.
Keller, Wm. L.: Ohio State M. J. **26:** 21, 1930.
Keller, Wm. L.: Ann. Surg. **76:** 549, 1922.
Lilienthal, H.: Ann. Surg. **70:** 43, 1919.
Lambert, A. V. S.: Ann. Surg. **99:** 944, 1934.
Meade, R. H., Jr.: Ann. Surg. **101:** 559, 1935.
Meade, R. H., Jr.: Surg., Gynec. & Obst. **60:** 216, 1935.
Martin, W.: Ann. Surg. **100:** 1096, 1934.
Pool, E. H., and Garlock, J. H.: Ann. Surg. **90:** 213, 1929.
Scrimger, F. A.: Arch. Surg. **19:** 1313, 1929.
Stenbuck, J. B.: Surg. Gynec. & Obst. **56:** 705, 1933.
Robinson, S.: Surg., Gynec. & Obst. **22:** 557, 1916.
Tuffier, Th.: Ann. Surg. **72:** 266, 1920.
Wangensteen, O. H.: J. Thoracic Surg. **5:** 27, 1935.
Wilensky, A. O.: Ann. Surg. **73:** 30, 1921.

THE END-RESULTS OF HIGH LIGATION AND INJECTION IN THE TREATMENT OF VARICOSE VEINS

HENRY H. FAXON, M.D., AND DAVID W. BARROW, M.D., BOSTON, MASS.
(From the Peripheral Circulatory Clinic of the Massachusetts General Hospital)

OUR disappointing results of the injection method alone in the treatment of varicose veins[1] led us to adopt high ligation as a preliminary procedure in certain selected cases in 1931 and since that time we have employed this operation as an adjunct to the injection treatment in 1,072 extremities. Our data can have little significance unless accompanied by the details of our method of treatment, and, to clarify the basis on which the work was done, the salient features in dealing with these cases are taken up under separate headings before our statistics are given.

SELECTION OF CASES

High ligation was considered as an essential part of the treatment in those cases in which incompetence in the valves of the main saphenous trunk in the thigh could be demonstrated. The presence or absence of incompetent valves in the main trunk was determined by the findings of the Trendelenburg test[2] and the Schwartz test as originally described by Chevrier.[3] The details and significance of these procedures have previously been reviewed by one of us[4] and, as the fundamental factors in the study of varicose veins which they reveal are already familiar to those interested in this subject, further elaboration of these tests at this time seems unnecessary. It is not possible for us to state exactly what percentage of the cases reporting to the Clinic showed an incompetent main trunk, but our impression is that in at least 80 per cent of the cases in which the varices were of any appreciable size this finding was present.

TECHNIQUE OF HIGH LIGATION

The details of our technique of this operation were reported in 1934[4] and we have found no occasion for altering the procedure as originally described. The most important feature is the ligation of the long saphenous vein *at its junction* with the femoral as stressed by Homans.[5] Of almost equal importance is the separate division and ligation of at least the three highest branches of the saphenous vein together with an excision of 2 cm. of the main trunk below the ligature. Retrograde injection with a sclerosing solution of the distal segment before this is tied off, as suggested by Moszkowicz,[6] has been practiced in 90 per cent

Received for publication, December 30, 1937.

of the cases. In the earlier cases on which high ligation was carried out, we frequently made the mistake of ligating the vein well below the foramen ovale. "Faulty technique" is the term we have employed below to designate those cases in which this or any other operative error was made. We believe that in order to insure the ligature's being placed at the proper level the anterior surface of the femoral vein must be visualized at the time of operation, and it has been most instructive in the thirteen cases in which we have been forced to do the operation a second time at a higher level to see how extensive is the collateral which rapidly develops if any proximal saphenous stump is left behind at the original operation. The only cases in which we believe the procedure is contraindicated are those in which the superficial veins compensate for a deep circulation that has been impaired by a previous phlebitis; those showing active inflammation in the groin; and those in which hemolytic streptococci can be demonstrated in a complicating ulcer.

INJECTIONS FOLLOWING HIGH LIGATION

It was carefully explained to each patient that the operation was but one phase in the treatment of their varicosities and that for a satisfactory result it was essential that they report to the Out-Patient Department for a sufficient number of injections with quinine hydrochloride and urethane to obliterate all remaining unthrombosed veins. Despite our admonitions, however, a large number of patients failed to complete their required course of injections, apparently feeling that these were most uninteresting as compared to their more dramatic experience with surgery, and being well satisfied with the relief of symptoms which operation alone had afforded.

OTHER ADJUNCTS IN THE TREATMENT OF VARICOSITIES

A definite, although relatively small, percentage of the cases showed upon examination incompetence in the valves of the communicating branches between the deep and the superficial venous systems of sufficient degree to jeopardize the results in the treatment of the cases unless some step beyond high ligation and injection was carried out. These cases in most instances gave a history of a previous deep phlebitis and we have found it necessary to secure and divide these communicating branches by operation if a satisfactory result is to be obtained in this group of patients. The methods of accomplishing this have been outlined by one of us[7] and are to be reported later from this Clinic in more detail.[8]

Another relatively small group of the cases showed involvement of the short saphenous system in conjunction with varicosities of the long saphenous; and in the treatment of these patients ligation of the short saphenous vein in the popliteal space was carried out when this main trunk was shown to have incompetent valves.

METHOD OF SECURING FOLLOW-UP DATA

In order that there might be complete uniformity in the evaluation of the present status of each case, one of us (Barrow) personally questioned and critically examined each of the patients included in our statistics. All the patients who had undergone the operation of high ligation at least 1½ years prior to this follow-up were requested to return. Two hundred and twenty-eight patients reported for examination and the 218 patients who failed to respond are not included in our figures nor is any inference drawn from their persistence in remaining away. One hundred and thirty-seven patients of the 228 reported in the statistics had varicosities of both legs requiring bilateral high ligation so that 365 operations are represented by this group. We feel that any "follow-up" of such a group of cases attempted before at least 1½ years from the time of operation will lead to false conclusions. Although 1½ years represents the minimum period in this series, in some instances it has been as much as 5 years since the patient's operation, and the average elapsed time between high ligation and the present evaluation of the 228 cases was 2.9 years.

END-RESULTS

In order to make intelligible the classification of the 365 extremities into the three groups tabulated below in Chart I, a definition of terms is necessary. Criterion for the "perfect" result rating of Group 1 (55 per cent, or 200 extremities) was that the patient had enjoyed complete relief of symptoms following treatment and on examination showed all previous varicosities to be either completely thrombosed or free from any tension within those segments of veins from which blood could still be aspirated.

The standard for the "satisfactory" result rating of Group 2 (25 per cent, or 90 extremities) was that the patient had been symptomless since discharge; but, in contrast to patients in Group 1, these cases showed small but definite varices that detracted from the otherwise satisfactory cosmetic results. These veins were not manifestations of an incompetent superficial system, for by the Trendelenburg test they did not fill either from the main trunk above or from an incompetence in the communicating branches below.

The basis for the "failure" rating of Group 3 (20 per cent, or 75 extremities) was that the patient again showed varicosities that were of significance not so much because of their size as because they could be shown to represent stagnation in the superficial venous system. Despite the fact that 60 per cent of this group stated that they were better than before operation, we believe that with more time their improvement

will inevitably regress because of the persistence of the fundamental abnormality of venous back pressure that had not been adequately dealt with in the course of their treatment.

The persistence or recurrence of an ulcer after healing had taken place was considered *ipso facto* evidence of failure and placed that extremity in Group 3. Seventy-four patients, or one-third of the 228 patients represented in the present follow-up, showed ulcers upon admission or had suffered from them in the past; and of these 66, or 89 per cent, had secured complete relief from this complication following operation and injection.

It might seem that the interval between the time of treatment and the follow-up would have been an all-important determining factor in

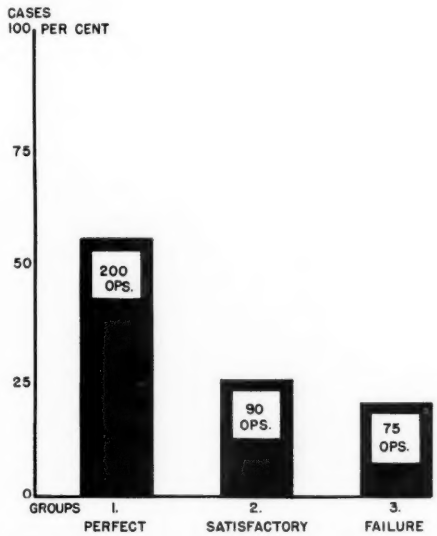


Chart I.—End-results of high ligation and injection, 365 extremities, Massachusetts General Hospital.

the end-result rating. However, our statistics showed that the average elapsed time of the follow-up for the failures (2.9 years) was essentially the same as for the perfect results (2.8 years).

Age and sex seemed to be irrelevant factors in the final result of treatment, and in the cases on which it was necessary to do a bilateral operation there was essentially the same percentage of success and failure as for the series as a whole.

Retrograde injection of the distal segment of the vein at the time of operation as carried out in 90 per cent of our cases made no apparent difference in the final rating. Ferguson states[9] that high ligation alone will be followed "as a rule" by a variable amount of thrombosis, which, according to De Takáts,[10] results in complete occlusion of the saphenous system in 10 per cent of the cases. The contrasting figure of 36 per cent

of our cases, which showed such extensive obliteration following operation and retrograde injection as to require no further injections, would strongly suggest that the supplementary use of a sclerosing solution at the time of operation definitely augments the natural tendency to distal thrombosis.

The extent of the thrombosis following operation seemed to have little bearing on the end-result, for 35 per cent of the perfect results required no subsequent injections, while this was true in 33 per cent of the failures. The average number of injections per patient following operation for the entire series, including those who required no injections, was 2.2, being essentially the same in each of the three groups and showing a striking decrease from the average number of 7 injections reported from this clinic[1] when the injections treatment alone was employed. Sixty-six cases on whom we carried out high ligation had previously undergone a series of injections that had failed to give permanent relief.

COMPLICATIONS

Wound sepsis of sufficient extent to prolong the anticipated hospital stay was present in 2 per cent of the cases, but only in the one cited below was this complication of serious proportions. An appreciable number of patients who were not delayed in their return to work showed some induration of the wound and a variable amount of extravasation of blood into the tissue.

One of the early cases in this series, already reported in detail,[4] died following extensive hemolytic streptococcus wound infection of a pulmonary embolus. In this instance we believe there were extenuating circumstances due to our inexperience with the procedure and improper after-care which contributed materially to the fatal outcome. Since these figures were compiled, we have had a second case in which death was presumably due to a pulmonary embolus, although this could not be confirmed as autopsy was refused. This patient was a man of sixty years of age, in apparent good health, on whom high ligation and injection had been carried out and been followed by an uneventful convalescence and discharge from the hospital. Eight days following operation he suddenly collapsed on the street and was taken to another hospital where he died. A third case of pulmonary embolus which did not prove fatal was diagnosed clinically. Although the reported statistics of this paper cover only 367 ligations, we have given here, because of the seriousness of this complication, our complete experience with pulmonary emboli to the present time in 1,072 high ligations.

A complication due to operative technique was found in one patient in whom the femoral vein was mistakenly ligated and injected by the operator in the belief that he was dealing with the long saphenous. Religation of the severed vein was necessary shortly after the original

operation because of hemorrhage and the patient subsequently showed marked edema of the entire leg which has slowly partially subsided in the course of the ensuing six months. This is the only case of hemorrhage in our complete experience with high ligation in which it was necessary to do a secondary operation to secure the bleeding vein.

DISCUSSION

A critical study of the failures of Group 3 leads us to believe that five factors were largely responsible for the unsuccessful outcome in these cases. In some instances a single one of these factors was at fault; whereas, in others, a combination of two or more were present.

1. *Faulty Technique.*—In 29 extremities, or 39 per cent of the failures, it was apparent at the time of the follow-up examination from the findings of the Trendelenburg test that our stipulations for a successful high ligation had not been carried out by the operator. In 13 cases in which a second operation was done above the level of the first, the failure of the original ligation to interrupt the main trunk at its junction with the femoral was confirmed by direct visualization. In these cases the persistence of a proximal stump of saphenous vein had failed to dispel the effects of back pressure; and, through the collateral circulation established by way of the branches of this stump (Fig. 1), the same faulty venous situation which had originally obtained had been reestablished. The high incidence of faulty technique was due in the earlier cases to our failure to fully appreciate the high level at which the saphenous vein joins the femoral, and no doubt the fact that many individuals from the rapidly changing house staff have done the operating in the majority of these cases has contributed in more recent cases to a repetition of the same error. Reoperation is indicated when it can be shown that the first attempt has been technically unsuccessful.

2. *Incompetent Communicating Branches.*—The presence of incompetent communicating branches will serve to permit the effects of back pressure in the superficial venous system to be exerted upon the lower extremity (Fig. 2). It was impossible at the time of the follow-up examination of the patients to segregate those cases in which incompetent communicating branches had been overlooked at the time of the first evaluation of the case from those in which the failure of the valves in the branches had developed subsequent to the time of high ligation. We feel that the former was the case in most instances, although we recognize that there is a well-marked diathesis in all patients with varicosities of any appreciable size toward the dilatation of apparently normal veins.

In 16 extremities, or 21 per cent of the failures, one or more persistent incompetent communicating veins were found in the lower leg; and in 19 extremities, or 25 per cent, the offending vein was above the knee, usually at either the junction of the middle and lower or middle and upper thirds of the thigh. We have had disappointing results in at-

tempting to secure thromboses of these communicating veins by injections and believe that some form of surgical approach to interrupt their continuity is indicated as the only effective method by which their untoward influence upon the saphenous system can be abolished.

3. *Short Saphenous System.*—An inadequately treated short saphenous system, when found in conjunction with varicosities of the long saphenous, will result in failure to permanently relieve the patient of symptoms as brought out in 5 of the cases in Group 3 (Fig. 3). This

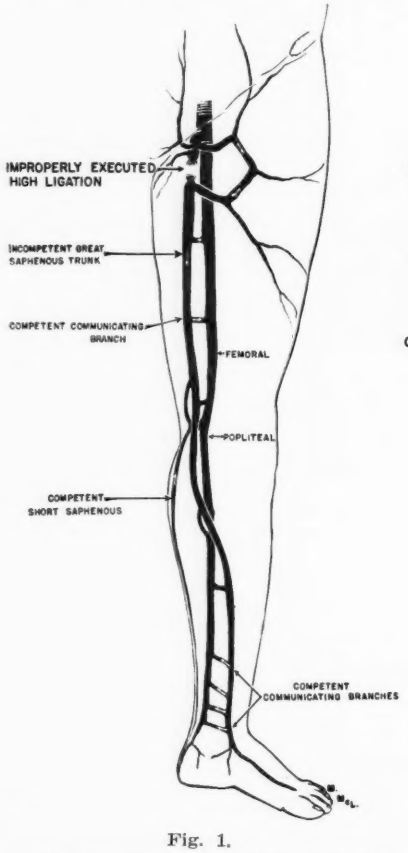


Fig. 1.

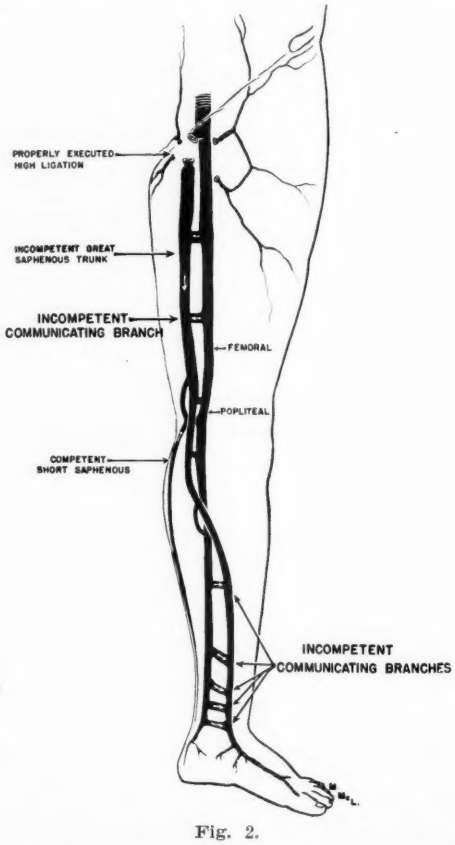


Fig. 2.

Fig. 1.—Diagrammatic illustration based on findings at operation in certain cases of recurrences where the reestablishment of back pressure has taken place through the stump of the saphenous and its highest tributaries. Had the first ligation been properly carried out at the junction of the saphenous with the femoral vein, such recurrences would not have occurred.

Fig. 2.—Diagrammatic illustration of the findings in certain cases of recurrences where, although the high ligation has been properly carried out, the effects of the reversal of venous flow in the superficial system still manifest themselves through the incompetent communicating branches. A direct surgical attack of these branches is the only manner of effectively correcting this situation.

occurred in 3 extremities, or 4 per cent of our failures. When the main trunk of the short system is incompetent, we believe that ligation at the popliteal vein should be done on the same basis and with an observance of the same general principles that high ligation is carried out in the groin.

4. *Damaged Deep Circulation.*—In 2 cases that gave a history of deep phlebitis, there had occurred such obliteration of the deep veins that the varicosities had been forced to take over a very definite compensatory rôle in the venous return from the extremity. This situation should have been recognized at the time of the original examination by the proper evaluation of von Perthes modification of the Trendelenburg test and other measures previously reported in detail,[7] and no treatment of the veins should have been instituted. It is not surprising that

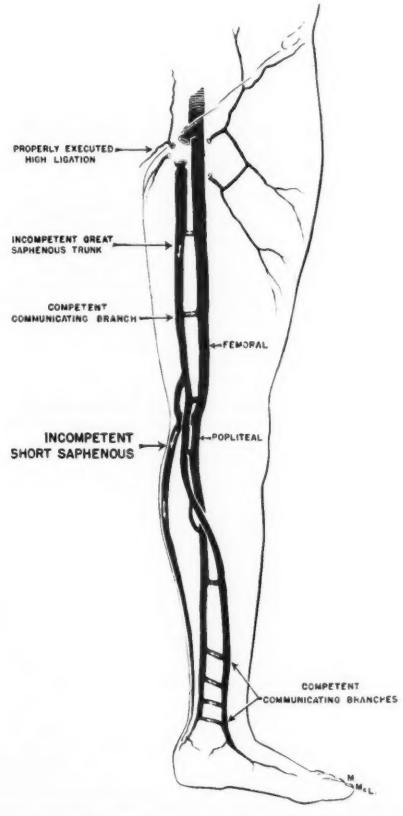


Fig. 3.—Diagrammatic illustration of the findings in certain cases of recurrences where, although the long saphenous vein had been adequately treated, an unrecognized varicose short saphenous system had been overlooked. When such short saphenous involvement is present, it must be properly handled at the time of the original treatment.

ligation and injection in these two improperly selected cases should have resulted in an ineffective extent of thrombosis of the veins and a moderate amount of aggravation of the symptoms. Although we formerly believed that, following a deep phlebitis, the superficial veins were frequently called upon to assume an important part in the venous return, more extensive clinical experience leaves us with the conviction that this is rarely the case.

5. *Postoperative Injections.*—Unless all varicosities that remain patent following high ligation are treated by subsequent injections, they will remain essentially unchanged or slowly enlarged. There were a definite number of patients in this series who failed to complete their course of injections and it was impossible to accurately determine at the time of our follow-up whether a few scattered varices were due to inadequate sclerosis of all varices at the time of the original treatment or to recurrences from recannulization of the thrombi. Although this latter is a fundamental tendency in Nature's process of repair, as brought out by Ochsner and Garside[11] and by Howard,[12] we feel that it is of little significance from a practical point of view unless the vein in question is subject to the hydrostatic pressure resulting from an uncorrected incompetent superficial system. We feel that the factor of inadequate postoperative injections played a relatively small part in the failures but a very real rôle in relegating an appreciable number of cases from the perfect results of Group 1 to the satisfactory results of Group 2.

SUMMARY

The end-result rating in 367 operations of high ligation in selected cases carried out in conjunction with the injection treatment of varicosities showed perfect results in 55 per cent of the cases; satisfactory results in 25 per cent; and failures in 20 per cent. The average elapsed time between operation and the follow-up examination was 2.9 years and in no instance was this interval less than 1½ years. The chief factors responsible for the recurrences in the group of failures were faulty operative technique, 39 per cent; complicating incompetent communicating branches, 46 per cent; short saphenous involvement, 4 per cent; and the improper selection of cases, 3 per cent.

CONCLUSIONS

1. Successful results in the treatment of varicosities may be obtained by high ligation and subsequent injections alone in at least 80 per cent of the cases in which there is an incompetent main saphenous trunk unassociated with involvement of the perforating branches or short saphenous system.

2. High ligation in these cases will not be effective unless carried out at the junction of the saphenous with the femoral vein.

3. The operation of high ligation carries with it a small but definite risk of major wound sepsis (2 per cent) and pulmonary emboli (0.3 per cent).

4. Direct operative approach is the only effective method of correcting the abnormal venous flow found in grossly incompetent perforating branches or extensive short saphenous involvement.

5. The incidence of recurrences depends primarily on the success of the original evaluation and treatment of the cases rather than on the elapsed period from the time of treatment.

6. Age, sex, the presence of bilateral varicosities, and the extent of thrombosis following operation play no significant rôle in the ultimate success or failure of treatment.

7. Retrograde injection of the distal segment of the vein at the time of operation makes no significant difference in the end-result rating, although it does apparently decrease the number of injections required after operation.

8. An adequate series of postoperative injections into all unthrombosed veins is essential if the best results are to be obtained.

REFERENCES

1. Faxon, H. H.: End-Results in the Injection Treatment of Varicose Veins, New England J. M. **208**: 357-361, 1933.
2. Trendelenburg, F.: Ueber die Unterbindung der Vena saphena magna bei Unterschenkelvaricen, Beitr. z. klin. Chir. **7**: 195, 1891.
3. Chevrier, L.: De l'examen du reflux veineux dans les varices superficielles, Arch. gén. de chir. **1**: 34, 1908.
4. Faxon, H. H.: The Treatment of Varicosities; Preliminary High Ligation of the Internal Saphenous Vein with the Injection of Sclerosing Solutions, Arch. Surg. **29**: 794, 1934.
5. Homans, J.: The Operative Treatment of Varicose Veins and Ulcers, Based upon a Classification of These Lesions, Surg., Gynec. & Obst. **22**: 143, 1916.
6. Moszkowicz, L.: Behandlung der Krampfadern mit Zucker-injektionen kombiniert mit Venenligature, Zentralbl. f. Chir. **54**: 1732, 1927.
7. Faxon, H. H.: Present Methods of Treating Varicose Veins, New England J. M. **216**: 327, 1937.
8. Linton, R. R.: Personal communication.
9. Ferguson, L. K.: Ligation of Varicose Veins Ambulatory Treatment Preliminary to Sclerosing Injections, Ann. Surg. **102**: 304, 1935.
10. De Takáts, G.: Ligation of the Saphenous Vein, J. A. M. A. **94**: 1194-1917, 1932.
11. Ochsner, A., and Garside, E.: The Intravenous Injection of Sclerosing Substances, Ann. Surg. **96**: 691, 1932.
12. Howard, N. J., Jackson, C. R., and Mahon, E. J.: Recurrence of Varicose Veins Following Injection. A Study of the Pathological Nature of the Recurrence and a Critical Survey of the Injection Method, Arch. Surg. **22**: 353, 1931.

VARICOSE VEINS, WITH SPECIAL REFERENCE TO TREATMENT BY LIGATION, STRIPPING, AND INJECTION

EDMUND HORGAN, M.D., WASHINGTON, D. C.

OVERDISTENTION of thin-walled veins in the subcutaneous tissue of the lower extremities with stretching and insufficiency of the venous valves is the beginning of the condition known as varicose veins. The condition progresses as structural changes in the vein walls produce hypertrophy, elongation, and tortuosity. The development of varicose veins limits the activity of the individual and in some instances prevents him from carrying on a gainful occupation, entering into sports, or engaging in the ordinary activities of life, such as walking, dancing, and so forth.

ETIOLOGY

The cause of varicose veins has been a subject of much discussion and conjecture, but it is generally conceded that a congenital weakness of the middle layer of the vessel wall is the primary factor. Other factors, such as standing, walking, and doing heavy laborious work for long hours without rest periods, tend toward the development of varicose veins from the inherent congenital weakness. Pregnancy and pelvic and abdominal tumors, such as fibroids, retroperitoneal tumors, etc., are causative factors when they obstruct the venous return from the lower extremities. Phlebitis and thrombosis occurring in the lower extremities during infectious diseases, such as typhoid fever, pneumonia, and influenza, or resulting from focal reactions following the removal of foci of infection, such as teeth, tonsils, gallbladder, appendix, hemorrhoids, and so forth, as well as those occurring as a postoperative complication after any other operation, may likewise induce the condition.

PATHOLOGY

In the congenital thin-walled vein there can be observed histologically a middle layer that is considerably thinner than normal. This layer is made up of muscle fibers and a larger amount of connective tissue. The muscle fibers do not have a regular course. They run in bands, some of which are circular, while others run in the longitudinal direction. When overdistention of such a thin-walled vein is caused by one of the factors enumerated above, the vein wall stretches and under the strain of distention the venous valves become incompetent. There is a tissue reaction in the vein wall to prevent greater distention and valvu-

Received for publication, October 21, 1937.

lar insufficiency. This reaction occurs mostly in the middle layer and histologically there is seen an increased production of fibrous tissue which causes hypertrophy of the wall of the vein. The connective tissue production also causes elongation and tortuosity of the vessel. The production of fibrous tissue in the vein wall may be so great that the vessel becomes inelastic, but before this stage is reached the valves have usually been almost obliterated. Under such conditions the blood will not flow freely through the veins and in some of the veins the blood may stagnate. This would have a tendency to favor and produce phlebitis and thrombosis within the vessel. As a result of the phlebitis and thrombosis, ulceration may occur. Trauma may produce phlebitis, thrombosis, and hemorrhage. The hemorrhage may be confined to the subcutaneous tissue, but in some injuries the skin is broken and there is a profuse loss of blood. Occasionally a distended varicose vein will cause necrosis of the skin over it and a spontaneous hemorrhage will result. This has been observed during pregnancy.

Some forms of phlebitis and thrombosis are associated with a local infection in the vein wall. This was described by Jacques,[1] who referred to it as a latent infection. The latent infection may be activated and may produce extensive phlebitis and thrombosis and, under some conditions, ulceration.

SYMPTOMATOLOGY

As the result of venous dilatation, venous hyperemia, and edema, there are discomfort and pain in the extremity. The pain varies in intensity according to the sensitiveness of the patient and the pressure within the distended vein. The mechanism of the pain is via the sympathetic nervous system and the spinal cord to the brain. The fibers of the sympathetic nerves are found in the external layer of the vein wall.

Where venous hyperemia is marked, there are often mild capillary hemorrhages which result in pigmentation of the skin as the blood pigment is taken up from the tissues. Where phlebitis is present, there are pain and tenderness along the course of the vessel involved. The pain is more marked in thrombophlebitis and may be so severe that the patient is unable to walk. Swelling of the lower extremity usually accompanies phlebitis and thrombophlebitis.

When a vein in the leg becomes thrombosed and the tissues of the lower part of the extremity become tense from the swelling, ulceration sometimes occurs. The pain associated with the thrombophlebitis, necrosis, and formation of the ulceration is very acute, particularly in the tissue surrounding the ulceration. This tissue presents all the signs and symptoms of an acute inflammatory process.

TREATMENT

In undertaking the treatment of varicose veins we must take into consideration (1) the extent of venous involvement, (2) a history of

or the presence of phlebitis in the deep or superficial veins, (3) a history of or the presence of thrombosis in the deep or superficial veins, (4) acute or chronic ulcerations, and (5) edema of the lower extremities. We must also consider pregnancy, obesity, cachexia, albuminuria, diabetes, senility, heart disease, and arterial hypertension before instituting any form of treatment. There is one condition that contraindicates all treatment for varicose veins; that is, where there has been a thrombosis with obliteration of the deep veins. Whatever form of treatment is undertaken, it is well to have the patient on a low caloric diet, to reduce the quantity of fluid intake to 1,000 c.c. a day, to avoid alcohol and tobacco, and to see that there is a daily evacuation of the bowels. Where the treatment is ambulatory, the patient should be instructed to arrange for rest periods during the day, in order to avoid the distention of the vessels that would result from standing for long hours. It is also advisable to instruct the patient not to walk long distances without a rest period.

The treatment can be divided into (1) bandaging, (2) rest, (3) the injection of a sclerosing solution, and (4) surgery.

Bandaging.—Bandaging is not a curative treatment, but if properly carried out it may prevent the varicosities from progressing and may prevent phlebitis, thrombosis, edema, and ulceration. The usual bandage is made of an elastic webbing. A stocking of lastex may be worn instead. These fabrics are compressive in their action on the superficial circulation and will prevent overdistention of the veins and edema in the subcutaneous tissues, as well as phlebitis, thrombosis, and ulceration. The compression bandage of whatever type should include the foot, ankle, and leg. Bandaging above the knee is usually not effectual and consequently is not desirable. The compressive type of bandage is sometimes contraindicated in large, brittle, inelastic veins, because the pressure would traumatize the vein by breaking the vessel wall.

Rest.—In the presence of phlebitis, thrombosis, marked edema, hemorrhage, and varicose ulcerations the patient should be ordered absolute bed rest with elevation of the extremities. Wet dressings which include the foot, ankle, and leg should be kept on continuously. For such dressings boric acid solution, salt solution, or aluminum subacetate solution may be used. The dressing should be soaking wet at all times, and an oil silk or rubber covering should be placed over the dressing in order to retain the moisture.

After the acute phase of the above conditions has subsided, treatment of the varices or the ulceration may be instituted. I shall not enter into a discussion of the care of ulceration, as this has been described in detail by McPheeters[2] in his monograph on varicose veins. When the ulcer has healed, the varicosities may be treated.

Injection.—For some years sclerosing solutions have been used in the treatment of varicose veins. Biniodide of mercury, urea and quinine

hydrochloride, sodium salicylate, sodium carbonate, sodium citrate, sodium chloride, glycerine, glucose, sodium morrhuate, and other substances have been employed. In selecting the sclerosing solution, one that does not cause clotting should be chosen. The solution should cause a sclerosing action on the intima of the blood vessel wall. With the vein nearly empty when the injection is made, the solution injected will become effectual if the vein is kept compressed by a bandage. If the solution is injected into a vein full of blood, it will be diluted and may prove ineffectual in sclerosing the vessel. It may also become ineffectual if the vein is not kept collapsed by a compression bandage for about twenty-four hours after the injection.

The injection of a sclerosing solution is not to be considered lightly, as death has followed its use. However, it is commonly employed, usually as an ambulatory treatment. Failures as high as 90 per cent

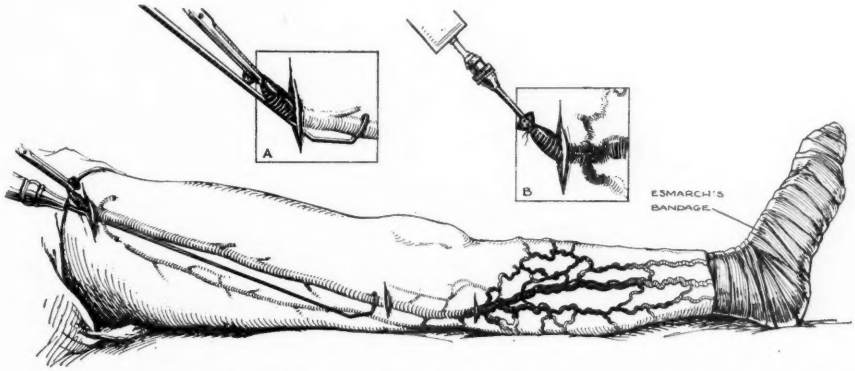


Fig. 1.—A drawing showing stripping of the long saphenous vein from the saphenous opening to the knee after the proximal end of the divided vein has been ligated. It also shows a small incision above the knee through which the vein has to be drawn after it has been stripped. *A*, shows the further stripping of the vein to a point below the knee; this may be done if the varicosities do not extend above the knee. *B*, shows the injection of the sodium morrhuate solution into the distal portion of the long saphenous to sclerose the tortuous varicose veins between the knee and the ankle.

have been observed one year after treatment in some series.[3] Many cases which apparently had a good result immediately following the injection treatment later have been observed to have a recurrence. No sclerosing solution should be injected into large, inelastic veins, when there is present an acute phlebitis or thrombosis, during the late months of pregnancy, or when there is an acute inflammatory area around a varicose ulceration.

In 1930 Rogers[4] pointed out that sodium morrhuate, first reported by him in 1916, has the effect of sclerosing the intima of veins without increasing the coagulability of the blood, so that there appears to be no danger of resulting embolism. As the result of his experimental studies, Ochsner[5] agrees with Rogers and others that sodium morrhuate (5 per cent) is an effective substance in the treatment of varicose veins,

and he is inclined to the view that it is the most efficacious substance for the purpose. Ochsner and Mahorner[6] studied the effect of sclerosing agents and showed that some of them not only destroyed the intima but at times produced a coagulation necrosis of the media of the vein.

Occasionally there are seen following the injection of varicose veins inflammatory reactions which produced phlebitis in the injected extremity or in the opposite one. Jacques[1] is of the opinion that some of the local reactions and periphlebitis are chemical in origin, but that in a large percentage of cases the lesion is an infectious one. He believes that such lesions arise from latent or "resting" infection in the wall of the affected varices. Such latent or "resting" infections may light up as the result of the injection of sclerosing solutions.

Surgery.—Various operations have been devised for the treatment of varicose veins. My own choice is a method which combines ligation, stripping, and injection. Under general or spinal anesthesia the procedure is carried out as follows: The leg, thigh, and groin are prepared by shaving, etc. When the patient is placed upon the operating table, the extremity is elevated at 15 degrees. An Esmarch elastic rubber bandage is applied to the foot and the ankle. A second Esmarch bandage is applied from the ankle to the knee. To the skin of the thigh and groin an antiseptic solution is applied. Sterile towels and sheets are arranged to protect the operative field from contamination. An incision is made obliquely over the saphenous opening; the long saphenous vein is exposed, divided between clamps, and the proximal end doubly ligated. A Mayo vein stripper is used to strip the vein almost to the knee. A second incision is made while the vein stripper is in place, so that the vein passing through the ring of the stripper can be easily identified. The stripped vein is removed from the thigh through the small incision and most of the vessel is cut off. Into the distal end of the vein a cannula is inserted and fastened by a ligature. Through the cannula there are injected into the vein and its branches below the knee 5 to 10 c.c. of a 5 per cent solution of sodium morrhuate. Just as the solution is about to be introduced into the vein, the Esmarch bandage which was applied around the leg is removed. When all the solution has been injected, the vein is ligated; the incisions closed; and a compression bandage, made by applying a thick layer of absorbent cotton and rolling over it snugly a wide Ace bandage, is placed around the leg from the ankle to the knee. After the compression bandage is applied, the Esmarch bandage is removed from the foot. Varicosities that are not completely obliterated by the above procedure may be injected with sodium morrhuate at a later date.

This method has given uniformly satisfactory results. The following case illustrates what can be accomplished by its employment:

A female, aged forty years, married, consulted me on August 26, 1935, on account of varicose veins. She stated that she was thirty-one years of age when she first

became pregnant. Her first baby was born on July 31, 1925. It was a full-term baby and delivery was normal. The child weighed seven and one-half pounds. She had not noticed any trouble with the veins of her legs during this pregnancy or immediately following it. She further stated that she had never had phlebitis following any infectious disease.

In April, 1926, she became pregnant a second time. During this second pregnancy, the patient noticed varicose veins in both of her legs below the knees. As her pregnancy advanced, the condition grew worse. The veins in her abdomen were also noticeable.

On January 30 and 31, 1927, she was delivered at full term of twin boys weighing eight pounds each. The deliveries were normal. Following these deliveries, the patient had a severe postpartum hemorrhage. She did not have phlebitis following delivery and the varicosities became much less prominent. Within three months the patient became pregnant again. During this pregnancy the varicose veins became very noticeable. On February 3, 1928, at full term, she gave birth to a boy weighing eight and one-half pounds.

For six years the patient did not become pregnant again, and she had no trouble with the varicose veins, although they were quite noticeable. She again became pregnant toward the end of 1933. During this pregnancy she had a great deal of trouble with varicose veins in both lower extremities, involving the legs, thighs, groins, labia, and lower abdomen. She went to full term and was delivered normally of a ten-pound boy in September, 1934. Following this pregnancy, the varicose veins in her legs were prominent and she had considerable discomfort and cramping when she walked.

In the spring of 1935 the patient went to Europe and while abroad did a great deal of walking. She stated that it was necessary for her to spend one day out of three in bed while in Europe on account of the discomfort from the varicose veins. The patient consulted me following her return from Europe. I advised her to be operated upon.

An operation was performed on her by me at Columbia Hospital on September 4, 1935, in accordance with the above described technique. Her convalescence was without incident.

In March, 1936, the patient became pregnant again. She went through a normal pregnancy with the exception of high blood pressure and albumin in her urine. She had no trouble whatever with the varicose veins. She noticed that she had much less swelling of her ankles than in the former pregnancies. On December 24, 1936, she went through a normal labor and delivered a ten-pound, fourteen-ounce boy. Following this last pregnancy, there has been no sign of any varicosities.

REFERENCES

1. Jacques, L.: Varico-Phlebitis and the Injection Treatment, Ann. Surg. **95**: 746-753, 1932.
2. McPheeters, H. O.: Varicose Veins, with Special Reference to the Injection Treatment, Ed. 3, Philadelphia, 1931, F. A. Davis Company.
3. Howard, N. J., Jackson, C. R., and Mahon, E. J.: Recurrence of Varicose Veins Following Injection: a Study of the Pathologic Nature of the Recurrence and a Critical Survey of the Injection Method, Arch. Surg. **22**: 353-376, 1931.
4. Rogers, L.: Intravenous Sclerosing Solutions, Brit. M. J. **2**: 120, 1930.
5. Oehsner, A.: Relative Value of Sclerosing Agents in the Treatment of Varicose Veins, South. Surgeon **2**: 217-224, 1933.
6. Oehsner, A., and Mahorner, H. R.: Studies of the Comparative Value of Intravenous Sclerosing Substances, Proc. Soc. Exper. Biol. & Med. **30**: 1180-1181, 1933.

SOME EXPERIMENTAL OBSERVATIONS RELATING TO VISCERAL PAIN

ROBERT M. MOORE, M.D., GALVESTON, TEX.

(From the Department of Surgery, University of Texas, Medical Branch)

IN VIEW of the importance of pain as a symptom, it is surprising that so little is known of the processes by which pain arises in clinical conditions. Accurate bedside observations and careful autopsy studies have combined to furnish an empiric knowledge of pain that is of great use in diagnosis. In the majority of instances, however, the mechanism of pain production remains a mystery.

Experimental studies of the causes of pain have been relatively few. There are obvious handicaps for those who seek to study pain by means of animal experimentation. Humane precepts forbid the use of conscious subjects, but with anesthetized animals how is one to know when pain endings have been stimulated?

Happily, during recent years, as a result of advances in knowledge of visceral neurology, there has been an awakened interest in the origins of visceral pain. In our own laboratory we have been engaged throughout a period of six years in a series of experimental studies of various aspects of pain sensibility. Observations made in experiments on more than 500 animals have been the basis for a number of brief reports in physiologic journals. It is proposed at this time to summarize these findings in the belief that they are of clinical interest. The report will be restricted to our own work since excellent reviews have been published by Kuntz (1934), Livingston (1935), White (1935), and others.

I. PSEUDAFFECTIVE RESPONSES TO INTRAARTERIAL INJECTIONS OF IRRITANTS AS A METHOD FOR STUDYING PAIN SENSIBILITY

Woodworth and Sherrington (1904) found that in the unanesthetized but decerebrate animal certain types of stimulation aroused movements simulating the outward expression of emotional states. For example, central stimulation of the sciatic nerve caused alternate movements of the limbs, dilatation of the pupils, opening of the mouth, retraction of the lips and tongue, snapping of the jaws, vocalization, either snarling or plaintive, and with these a transient increase of arterial blood pressure. The authors concluded that these "pseudaffective" reflexes result from afferent "impulses that, were the brain intact, would, we may presume, evoke 'pain.'" The destruction of the hemispheres and thalamus abolishes the neural mechanism of consciousness, but "leaves fairly intact the reflex motor machinery whose concurrent action is habitually taken as an outward accompaniment or expression of an in-

Received for publication, July 31, 1937.

ward feeling. When the expression occurs it may be assumed that had the brain been present the feeling would have occurred.'' Thus, by decerebration, one can dissociate the sensation of pain from its outward manifestations, and study in unconscious animals various factors which have to do with the origination and progression of impulses in pain fibers.

In our laboratory it was noted (Moore and Moore, 1932) that in animals anesthetized with sodium amytal to a sufficient degree to permit the performance of laparotomy without notable reflex disturbance, injection of an irritating solution into the lumen of the femoral artery invariably provoked a similar reflex response. Apparently pain endings were stimulated to elicit a pseudaffective reaction, the experiment differing from that of Woodworth and Sherrington in that they had destroyed the hemispheres and thalamus surgically; whereas, we had depressed the function of the forebrain with the anesthetic substance. The majority of the experiments to be reported at this time are based upon this occurrence of a pseudaffective reaction when an irritating solution is injected down the artery of a decerebrate or of a barbitalized cat.*

An interest in pain arising from arteries prompted us to make additional observations (Moore and Moore, 1933). It was soon apparent that the stimulation did not result from distention of the artery, for innocuous solutions could be injected rapidly without producing reflex effects; whereas, irritant solutions provided strong stimulation when injected drop by drop. Similarly, it was found that the afferent stimulation did not take origin from a spasm of the arterial muscle. By means of a roentgenographic technique (Moore, Williams, and Singleton, 1933) it was possible to visualize the femoral artery at the moment when a painful stimulation was in progress and to see that the artery might be widely dilated relative to the companion vessel of the opposite limb. Therefore, we were led to conclude that the irritating solution acted directly upon nerve endings.

In attempting to locate these pain endings, several significant observations were made. The absence of an appreciable reaction when the solution was injected centrally into a vein excluded distant structures. The occurrence of intense responses upon injection of irritants into visceral arteries, such as the hepatic artery, showed that the cutaneous pain endings were not essential. Moreover, if the solution was confined to the trunk arteries by ligation of their branches or by embolic obstruction of their branches, no reaction occurred. The experiments confirmed those of Odermatt (1922) and indicated that stimulation resulted only when conditions permitted the stimulating agent to reach the capillary bed in an effective strength. There has been no generally accepted

*All intraarterial injections were made with the needle directed distally and with a ligature proximal to the site of injection, so that the solution flowed toward the periphery in an empty arterial tree (Fig. 1*a*).

histologic demonstration of sensory nerve endings in the intima of arteries or in the capillary endothelium (Woollard, 1926; Kuntz, 1934). This fact, coupled with our more recent studies, has led to the conclusion that the pain endings are located in the intercellular spaces of the peripheral tissues where they are reached by the irritant as a result of its rapid diffusion through the capillary wall (Fig. 1*b*).

If this conclusion is correct, the sensibility is not arterial but resides in the tissues adjoining the capillary bed. Intraarterial injection is the

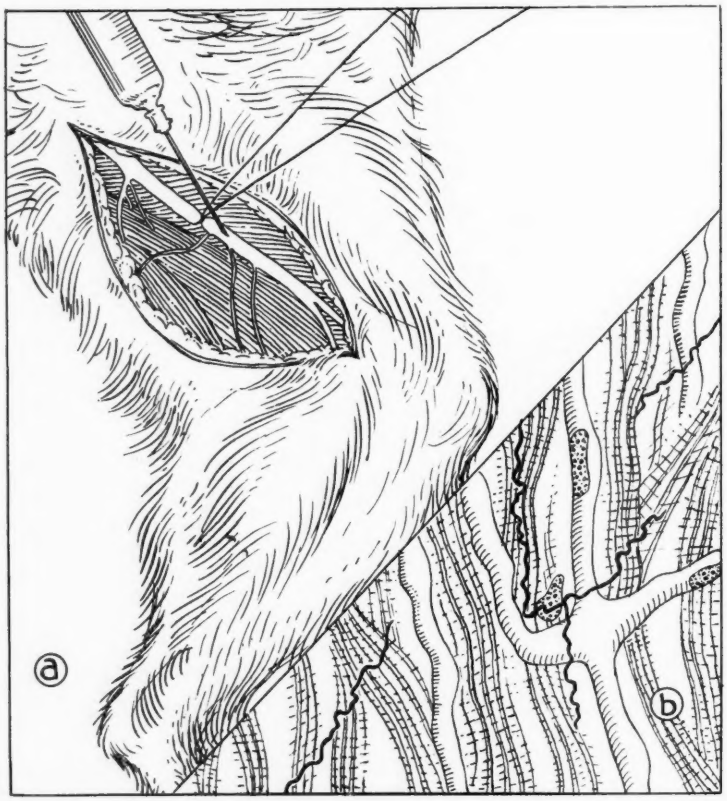


Fig. 1.—*a*, Method of intraarterial injection. The irritant is injected distal to a ligature so that it passes to the periphery through an empty arterial tree. *b*, Diagram of nerve endings in intercellular spaces of heart muscle (after a photomicrograph by Stöhr, 1928). Irritants injected by way of an artery apparently diffuse through the capillary wall to act upon such endings.

most effective means of stimulating these pain endings, however, probably because the stimulating agent is distributed to act on a large number of receptors at one time. We have observed repeatedly that a solution evoking signs of reflex stimulation when administered in this manner may fail to do so when injected directly into the tissues, a fact also noted by Burget and Livingston (1931). Therefore, most of our experiments have been based upon intraarterial injections of solutions of various kinds.

II. PAIN SENSIBILITY OF ARTERIES

In some instances the intraarterial injection of a caustic, such as strong acid or alkali, provides sensory stimulation when the solution is confined to the large vessels. That the noncaustic irritants we have ordinarily used serve to stimulate, but do so only when they are permitted to flow distally into the capillary bed, suggests that pain endings are absent from the intima of the arteries and that the caustic solutions erode the vessel lining to reach afferent nerve endings demonstrable histologically in the outer coats. In our experience local stimulation by caustics has resulted more often from injections into veins, possibly because they have a thinner wall. Clinically it is observed that solutions which elicit local pain when given intravenously quite often cause thrombosis of the injected vein, another fact which can be construed to indicate that the agent has destroyed the intima and invaded the outer layers of the vascular coat.

Surgeons frequently note pain incidental to mechanical manipulation of arteries. It has been suggested that this sensitivity to trauma is a function of the periarterial plexus (Odermatt, 1922). In our experience when manipulation of arteries has given rise to reflex activity, examination revealed the presence of a visible nerve which had been traumatized along with the artery. In cases in which the blood vessel had been carefully isolated from all accompanying nerve trunks it was found that neither ligation, clamping, stretching, puncture, nor any other form of mechanical manipulation gave rise to signs of reflex disturbance. The peripheral nerve branches are distributed with the peripheral arteries. Frequently the nerve is in contact with the wall of the artery and its branching takes place on the surface of the vessel. Under such conditions it may be impossible to manipulate the artery without injuring the nerve. The pain which arises from mechanical trauma, in our opinion, is properly explained on this basis. Such pain results neither from stimulation of nerve endings nor from a stimulation in the artery proper, but arises from physical injury to nerve fibers which are accidentally included in the manipulation.

We are inclined to minimize the importance of distention of arteries as a mechanism giving rise to painful sensation (Moore and Moore, 1933). We have produced visible distention of the femoral artery in amytalized animals by rapid injection of normal saline without eliciting any appreciable pseudaffective response to indicate that pain fibers had been stimulated. Knapp (1929) arrived at a similar conclusion.

Spastic contraction of arteries is often accompanied by pain. There is no proof, however, that the spasm itself is painful. In our experiments the pain arising from injections of barium salts was neither abolished nor appreciably diminished by previous or simultaneous injections of large doses of vasodilator substances, such as nitroglycerine or acetylcholine. The spasm of Raynaud's disease is the result of ex-

aggerated sympathetic vasoconstrictor activity and an identical form of spasm can be produced by administering adrenalin which stimulates the vasoconstrictor endings. But adrenalin does not cause pain when given by intraarterial or any other mode of administration. All forms of arterial spasm result in a proportionate ischemia. The spasm produced by adrenalin causes only momentary ischemia; whereas, that of Raynaud's disease may be maintained for hours until such profound chemical changes occur in peripheral tissues that gangrene results. It will be shown that these chemical changes can affect nerve endings. We are not in a position to deny that arterial spasm is ever of itself painful, but we are inclined to believe that it is relatively less important in the production of pain than are the chemical changes which result from the spasm.

III. PAIN SENSIBILITY IN SOMATIC AND VISCERAL TISSUES

In view of the rich supply of sensory endings in cutaneous areas, it might be presumed that reflex signs of painful stimulation following the injection of an irritating solution down the femoral artery arise from a stimulation of pain receptors in the skin. The cutaneous pain endings are not the sole source of the sensibility, however, for an intense pseudaffective reaction is elicited when a similar injection is made into an artery supplying a visceral organ. When, for example, 1.5 c.c. of the solution is injected into the hepatic artery of an amytalized cat, a marked reflex display makes its appearance. The animal struggles; it becomes hyperpneic; it tosses its head from side to side, and in many instances there is audible vocalization. The reaction appears within 1.0 to 1.5 seconds after the beginning of the injection and its duration varies from 5 seconds in some animals to 30 seconds in others. Profound anesthesia is required to prevent its occurrence.

In the initial study (Moore and Moore, 1933) 200 intraarterial injections of an irritant were made in approximately 100 animals. The usual result was a surprisingly strong reflex motor reaction following injection of any of the irritants used by way of any artery. The sensibility in question is therefore widespread. It is more acute in the tissues of the extremities than in those of visceral organs. In 93 instances an irritant was injected into an artery of an extremity. In all cases a pseudaffective reaction appeared and in 77 instances it was of great intensity. On the other hand, in 68 cases an irritant was injected into an abdominal artery of visceral distribution (hepatic, splenic, superior mesenteric, renal), with response of full intensity in only 13 cases, of moderate intensity in 35, and absent or questionably present in the remaining 20. Even when the reaction was slight, however, the stimulation was of necessity considerable since the animals were anesthetized to a degree which permitted ordinary surgical procedures without notable reflex disturbance.

In a more recent series of experiments (Moore and Singleton, 1935), injections of irritants into the myocardium by way of a coronary artery invariably provoked a marked reflex reaction and moderate responses were elicited from the lungs by injections into the pulmonary aorta.

Throughout this series of experiments there was evidence of strong stimulation of pain elements when an irritating solution was injected by way of any artery. The study as a whole justifies the conclusion that some degree of pain sensibility is present in all organs.

IV. PERIPHERAL PATHS OF PAIN FIBERS SUBSERVING THIS SENSIBILITY

Determination of the peripheral nerves which must be cut to prevent the reaction to an intraarterial injection makes it possible to map the peripheral course of the pain fibers to the region supplied by a given artery (Moore and Singleton, 1933). In this manner it can be shown that the fibers which end in relation to the capillary bed of the femoral artery pass to the spinal cord by way of the peripheral branchings of the spinal nerves, such as the sciatic and femoral nerves. Section of all trunks of the lumbosacral plexus abolishes the reaction from injection of the femoral artery. No appreciable number of the fibers ascend the artery for any great distance, for periarterial neurectomy does not abolish the response. A similar scheme of sensory innervation applies to the brachial artery. In each instance, femoral or brachial, sensory nerves join the artery at intervals in its course, for distribution to the peripheral tissues. Periarterial neurectomy at the root of the extremity, at best, anesthetizes only a small portion of the extremity. It should not be recommended, therefore, to abolish the pain accompanying peripheral arterial disease.

Either the upper or lower extremity, moreover, is rendered totally anesthetic to intraarterial injections when a sufficient number of posterior spinal nerve roots are sectioned. This indicates that pain fibers enter the spinal cord by way of the posterior roots only, as stated in the Bell-Magendie law, notwithstanding frequent claims to the contrary.

When irritating solutions are injected into the abdominal organs by way of their arteries, pain reactions are aroused. By determining which nerves must be cut to prevent these responses, it has been possible to determine the paths of the pain fibers to certain organs (Moore and Singleton, 1933). Fig. 2 illustrates these paths in the cat. The vagal cords at the cardia of the stomach contain motor and secretory fibers and also include afferent fibers which are instrumental in the production of vomiting (Walton, Moore, and Graham, 1931). Our experiments show, however, that the vagi contain no pain fibers from the abdominal viscera. The sympathetic trunks, lying at each side of the aorta (but projected laterally in the diagram, Fig. 2), give off "splanchnic" branches to the viscera. These are the pain nerves for the abdominal organs. Each organ receives its blood supply from the aorta. As its

artery leaves the aorta, it becomes ensheathed with nerve fibers from the adjacent sympathetic trunks. These fibers run with the artery to enter the organ at its hilus. Periarterial neurectomy performed upon the pedicle of an abdominal viscus does destroy the innervation of the organ, paralyzing its blood vessels and rendering it anesthetic. In this respect the nerve paths to the viscera differ from those to the extremities.

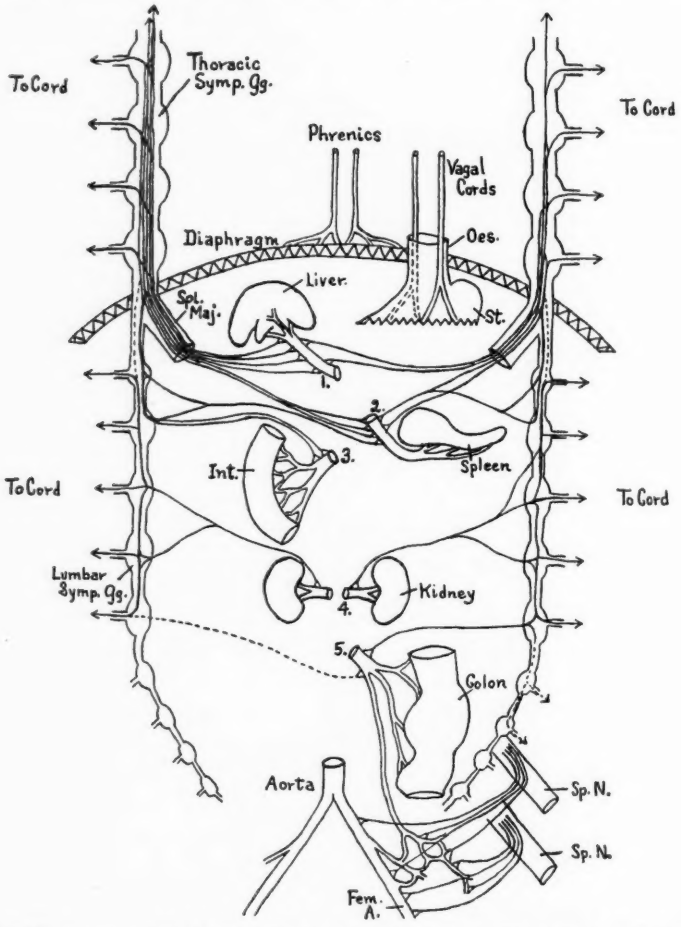


Fig. 2.—Diagram of peripheral paths of pain fibers accompanying the arteries to the abdominal viscera of the cat (see text). These fibers subserve local or "splanchnic" pain. Arteries: *1*, hepatic; *2*, splenic; *3*, superior mesenteric; *4*, renal; *5*, inferior mesenteric. (From Moore and Singleton: Am. J. Physiol. **104**: 271, 1933.)

The pain fibers from the liver and spleen course along their respective arteries to join the major splanchnic nerves and continue by way of these nerves to reach the spinal cord in the lower thoracic region. Pain fibers from the kidneys and intestine pass to the sympathetic trunk by one of its abdominal or minor splanchnic branches and enter the spinal cord, at least in part in the lumbar region. These paths, shown in Fig. 2, appertain in the cat. In man the details may differ, but it is logical to presume that the same general arrangement applies.

When the sympathetic trunks and their splanchnic branches are removed, the abdominal organs are rendered anesthetic, although the vagus and phrenic nerves are left intact. In making this statement we are excepting the parietal peritoneum, which receives its nerve supply from somatic or spinal nerves ending in the overlying body wall. It is not anesthetized by lumbar sympathectomy and splanchnotomy. Its sensibility, however, can be excluded in the experiments outlined above. For example, the spleen of the cat floats freely in the omentum without ligamentous attachment to the parietal peritoneum or to the body wall. Yet, when an irritant is injected into the splenic artery, a pseudaffective reaction occurs. Similarly, the kidney can be freed in its bed, its peritoneum stripped and the organ lifted up, isolated from the body except for its pedicle containing artery, vein, and perivascular nerves and lymphatics. An injection of the organ through its artery still evokes a reflex reaction, although it has been isolated from the adjacent somatic structures. Thus the viscera possess a pain sensibility which is independent of the parietal peritoneum and which is subserved by visceral fibers which pass to the spinal cord by way of the sympathetic and splanchnic trunks.

In a number of animals in which all sympathetic and splanchnic paths from the abdomen had been previously interrupted a laparotomy was done under light sodium amytal anesthesia. There was constant reflex activity during the incision of the skin and again during the cutting of the submuscular fascial layer (the posterior rectus sheath fused with the parietal peritoneum). But when this work in the domain of the intercostal nerves was completed and the abdomen was opened, it was found that the abdominal contents could be traumatized freely without causing the slightest reflex effect. Thus, in respect to their afferent components, the sympathetic trunks and their splanchnic branches are the true pain nerves of the abdominal organs.

We have injected irritants into the heart muscle by way of the coronary arteries (Moore and Singleton, 1935). Injection of 0.5 c.c. of 20 per cent lactic acid in decerebrate animals caused instantaneous and very marked reflex activity associated with a rapidly progressing black discoloration of practically the entire wall of the ventricle of that side. This was followed in five or ten seconds by acute dilatation of the ventricles, the resulting diminution in cardiac output rapidly leading to asphyxia. By this technique we believe we stimulated the same pain endings as are affected in coronary thrombosis or occlusion.

The cervicothoracic sympathetic trunk in the cat differs from that of man in that the inferior ganglion is fused with the upper two thoracic ganglia to form the large so-called stellate ganglion. Injection of lactic acid into the left coronary artery in fifteen cats in which the left upper thoracic sympathetic chain was intact caused, in every instance, an immediate and marked pain reaction. Since in a number of these

animals both cervical sympathetic trunks had been removed in their entirety, it was concluded that bilateral cervical sympathectomy does not interrupt the pain fibers which supply the left coronary artery. In contrast, injection into the left artery caused no reflex effect whatever in any of nine animals in which the left upper thoracic trunk had been removed from above the stellate ganglion to the seventh rib, although in these animals the cervical trunks and the right thoracic trunk were left undisturbed. Apparently all of the pain fibers to the tissues supplied by the left coronary artery pass to the spinal cord by way of the left upper thoracic sympathetic trunk. Similar experiments have shown that the tissues supplied by the right coronary artery are anesthetized by resection of the right sympathetic trunk and that the preponderance of these fibers pass to the cord by way of the thoracic segments.

Demonstration that the pain fibers from the coronary arteries enter the sympathetic trunk in the upper thoracic region confirms the belief of Mixter and White (1931) that resection of the upper thoracic ganglia is of more value in relieving the pain of angina than is cervical sympathectomy. The purely homolateral sensory innervation of each coronary artery is, however, a novel finding. Perhaps its anatomic basis lies in the fact that the deep cardiac plexus which supplies the coronary arteries is composed of right and left parts having very slight intercommunication, each part receiving its central connections from the sympathetic trunk of the same side. If this scheme of homolateral afferent innervation applies in man, before attempting to relieve coronary pain one must determine from the electrocardiographic tracing which coronary artery, right or left, is the one diseased. Once this point is established, resection or injection of the upper thoracic portion of the homolateral sympathetic trunk should be the operation of choice.

V. CHEMICAL STIMULATION OF PAIN RECEPTORS

Since it has been suggested from time to time that chemical changes in diseased tissues may initiate pain, we interested ourselves in determining the chemical properties which can serve as a stimulus to pain endings (Moore, Moore, and Singleton, 1934).* Isotonic or normal sodium chloride solution (0.9 per cent) can be injected by way of any artery in any quantity and at any rate without producing painful stimulation. The injection may be so rapid as to distend the artery visibly. If, however, one injects a series of solutions of progressively increasing sodium chloride concentration, it is found that when the concentration reaches 3.0 per cent or half-molar strength strong stimulation of pain elements results. This is true for all salts tested, and it can be stated

*It was found that in cats of average size an injection of 1.5 c.c. in the case of the femoral artery (or 1.0 c.c. in case of the brachial) sufficed to irritate the capillary bed and to elicit a pseudaffective reaction when a threshold concentration of the irritant was used. Therefore, in testing sensibility, this volume of solution was injected.

as a general principle that any hypertonic solution with total salt content approximating half-molar is irritating to pain endings.

Upon injecting a series of solutions of progressively diminishing sodium chloride concentration, it is found that painful stimulation occurs when the content falls to 0.3 per cent or one-third isotonic. This property, in turn, is common to all decidedly hypotonic solutions, distilled water giving strong stimulation.

Normal or isotonic saline becomes irritating when it is made acid or alkaline in reaction. By means of injections of a series of carefully adjusted buffer mixtures, it has been possible to demonstrate that normal saline becomes irritating to pain endings when the acidity reaches pH 6.3, a very slightly acid solution. On the other hand, when alkali is added to saline, irritation does not result until the alkalinity reaches the degree indicated by pH 9.2. Thus pain endings are more sensitive to acid than to base.

An isotonic solution which is neutral in reaction, moreover, may be irritating if it contains one of certain ions (Moore, Moore, and Singleton, 1934). Thus, although a half-molar solution of sodium chloride or of calcium chloride or of lithium chloride is required to irritate, chlorides of some elements evoke stimulation of pain endings in much lower concentration. For example, potassium chloride and rubidium chloride stimulate in twentieth-molar solution; whereas, barium chloride provides stimulation in fiftieth-molar concentration (Table I). Since the chloride anion is common to both groups, this difference is obviously a property of the metallic cation. Chlorides, therefore, fall into two groups, those of the sodium chloride group (LiCl, NaCl, CsCl, $MgCl_2$, $CaCl_2$, and $SrCl_2$) which are irritating only when present in high concentration and then as a result of an osmotic or salt effect, and those of the potassium chloride group (KCl, RbCl, and $BaCl_2$) which provide strong stimulation in concentrations so low as to indicate a specific effect of the positive ion.*

Still a third group of chlorides may be distinguished. This group includes $MgCl_2$, $CaCl_2$, and $SrCl_2$. Although belonging to the sodium chloride group in that they themselves provide stimulation only in high concentration, they exhibit an additional action. Their presence prevents or antagonizes the stimulating action of the salts of the potassium group (Moore, 1934). Thus, whereas an isotonic mixture consisting of 3 parts of KCl and 7 parts of NaCl is highly irritating, an isotonic mixture containing 7 parts of KCl and 3 parts of $MgCl_2$ fails to stimulate. The magnesium salt apparently protects the pain endings from the harmful effect of the potassium ion. Similarly, magnesium compounds antagonize the irritant action of rubidium, of barium, of acid, of alkali, and of distilled water.

*Similarly, testing a series of sodium compounds, it was found that the citrate anion possesses a marked irritating power (Table I).

TABLE I

MINIMUM CONCENTRATIONS OF VARIOUS SALTS STIMULATING PAIN RECEPTORS ON INTRAARTERIAL INJECTION

REAGENT	MOLAR CONCENTRATION REQUIRED FOR STIMULATION			
	SALT	CATION	ANION	TOTAL IONS
Chlorides				
Sodium chloride	0.51	0.39	0.39	0.79
Lithium chloride	0.47	0.36	0.36	0.72
Cesium chloride	0.45	0.35	0.35	0.70
Calcium chloride	0.41	0.28	0.55	0.83
Magnesium chloride	0.295	0.20	0.40	0.60
Strontium chloride	0.19	0.12	0.24	0.36
Potassium chloride	0.05	0.04	0.04	0.08
Rubidium chloride	0.05	0.04	0.04	0.08
Barium chloride	0.02	0.02	0.03	0.05
Sodium Salts				
Sodium chloride	0.51	0.39	0.39	0.79
Sodium bromide	0.39	0.31	0.31	0.62
Sodium iodide	0.33	0.27	0.27	0.53
Sodium nitrate	0.33	0.25	0.25	0.50
Sodium thiocyanate	0.33	0.24	0.24	0.48
Sodium acetate	0.33	0.23	0.23	0.46
Sodium sulfate	0.32	0.33	0.16	0.49
Sodium fluoride	0.12	0.10	0.10	0.20
Sodium citrate	0.06	0.11	0.04	0.14
Potassium Salts				
Potassium chloride	0.04	0.04	0.04	0.08
Potassium nitrate	0.10	0.08	0.08	0.16
Potassium bromide	0.04	0.04	0.04	0.07
Potassium iodide	0.03	0.03	0.03	0.05

The similarity of these results to those obtained by physiologists in studies of irritability of unicellular organisms suggests an interpretation in terms of the permeability of the nerve membrane (Lillie, 1923). The cell membrane is freely permeable to water. Water passes rapidly into the cell or out of the cell in the direction of higher salt concentration. Thus, when a nerve ending is bathed in a hypertonic solution, the excess salt outside the structure effects a rapid passage of water out through the nerve membrane. The nerve ending is rapidly shrunken to the point of injury when irritation of the nerve results and pain is felt. Conversely, when a cell is bathed in a hypotonic solution, excess water without the cell flows rapidly toward the higher salt concentration of the interior. This sudden swelling of the pain receptor results in stimulation. Acids and alkalies penetrate the cell membrane to give rise to stimulation. The ions of the potassium-rubidium-barium group are known to penetrate the cell membrane many times as rapidly as do the ions of the sodium group and to effect stimulation through chemical change and swelling. In contrast, magnesium compounds have a protective influence which physiologists term "stabilization" of the cell membrane. They seal the membrane and make it temporarily impermeable, thus preventing the deleterious effects of water, acid, or potassium. This magnesium action on the pain ending is similar to the supposed action of

narcotics, which render the nerve membrane impervious and thus make the receptor relatively indifferent to environmental changes.

It is of interest to consider what these results may suggest with reference to possible chemical origins of pain in disease conditions. It is doubtful that in pathologic states the fluctuations of salt content are of sufficient extent to account for painful stimulation. Moreover, rubidium and barium ions are not normal constituents of the living body. Potassium, however, is important in the economy of life. Because of its propensity for rapid penetration of cell membranes, the bulk of the potassium under normal circumstances is found concentrated within the cells. When cells are injured, as in inflammation, these potassium stores are poured out into the intercellular fluids which bathe the nerveendings. Various investigators (Häbler and Hummel, 1923; Reimers, 1932) have reported potassium content in inflammatory exudates, in necrotic tissue, and in pus which greatly exceeds that concentration shown in Table I to be capable of stimulating pain elements.

The degree of alkalinity indicated by pH 9.2 can scarcely arise in the living body. Moreover, the blood is so admirably buffered that the slight acidity represented by pH 6.3 cannot develop in the presence of a normal circulation. A different state of affairs exists, however, when tissues are deprived of their proper circulation. In this connection experiments will now be described which indicate that cardiac muscle or skeletal muscle contracting under conditions of oxygen lack actually develops an acidity which exceeds the threshold found sufficient to produce painful stimulation.

VI. ACID PRODUCTION IN THE FUNCTIONING HEART UNDER CONDITIONS OF ISCHEMIA

Lewis, Pickering, and Rothschild (1931) concluded that in ischemic contraction of skeletal muscle pain results from a stimulus which is derived from the accumulation of some product of physiologic processes. Katz (1935) has concluded that anginal pain arises from the accumulation of a metabolic product which "appears to be acid in character." Meyerhof and Lohmann (1926) found that frog muscle may attain an acidity as great as pH 5.6 on complete fatigue. Dawson and Bodansky (1931) demonstrated that perfusion of the mammalian heart may be interrupted for a period sufficient to render subsequent washings as acid as pH 5.3. In view of these findings, the experiments described in Part V of this report, indicating that pain endings are stimulated by intra-arterial injections of solutions as weakly acid as pH 6.3, suggest that pain arising in ischemic tissues is acid in origin. However, since the observations of Meyerhof and Lohmann were made on washings of excised muscle and those of Dawson and Bodansky on the isolated heart, it seemed desirable to attempt to measure the accumulation of acid in ischemic tissues under less artificial conditions.

For this purpose we have determined, in a series of animals, the acidity of blood obtained from the veins of the functioning heart at varying intervals after ligation of both coronary arteries (Moore and Greenberg, 1937). The experiments were performed upon cats and dogs anesthetized with Dial (Ciba). Under artificial respiration the thorax was opened, the pericardium was entered, and a ligature was passed beneath the stem of each coronary artery proximal to its first major branch (Fig. 3). On tying these ligatures the ventricles were deprived of virtually their entire supply of arterial blood.

After ligation of both arteries, the contractions of the heart rapidly emptied all blood from the coronary veins. Therefore, in order to obtain a sample of coronary venous blood after the prescribed period of ischemia, it was necessary to confine blood in the veins by ligating the chief tributaries of the coronary venous sinus immediately after ligating the coronary arteries (Fig. 3). The coronary venous samples consisted, therefore, of normally alkaline venous blood trapped in the veins at the moment of ligation admixed with acid blood added to the sample as the heart contracted, the first ingredient serving to dilute and to neutralize the second. It is obvious that any lowering of pH in such mixtures reflected a much greater fall in pH in the capillaries and tissue spaces of the laboring muscle.

Ligation of both coronary arteries invariably resulted in acute dilatation of both ventricles which made its appearance in from three to ten minutes after the arteries had been ligated. At the first appearance of ventricular dilatation, the venous samples were taken.

The coronary venous blood showed a marked lowering of pH; whereas, the lactic acid content was increased greatly. In a series of 18 successful experiments, the period of ischemia ranging from three to nine minutes, the actual fall in pH as indicated by comparison with blood from the vena cava varied from 0.22 to 0.81 pH units and exceeded 0.50 in 9 of the 18 experiments. In 3 animals the pH fell below 6.6 and in 1 animal it reached 6.4. We believe these pH values are the lowest ever reported for blood from the living animal. They illustrate how rapidly acid metabolites accumulate when functioning tissues are deprived of arterial circulation (Moore and Greenberg, 1937).

As shown above, the coronary venous sample was in reality a mixed sample and the lowering of its pH to 6.6 or below indicated a much greater change in the cardiac muscle. Again, the chemical change was minimized because of the brief duration of the experiments. The blood samples were taken after a few minutes of ischemic contraction on account of impending ventricular dilatation. The individual muscle fibers were not completely exhausted, but were still contracting at the moment the samples were drawn. In the clinical case of myocardial infarction, however, a less extensive area of the heart being involved, the organ as a whole may continue its function for many hours while the infarcted

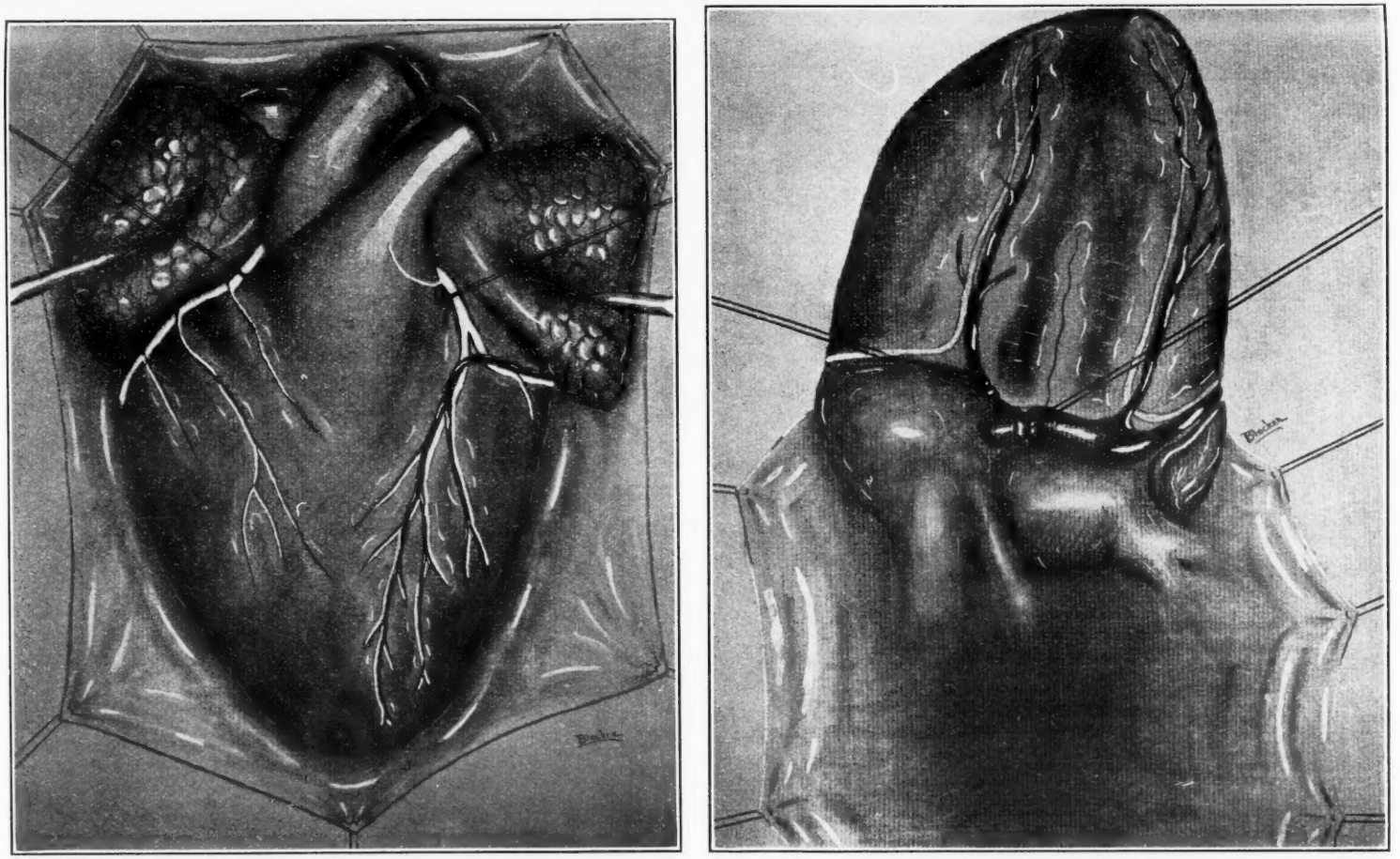


Fig. 3.—Method of studying acid production in the ischemic heart. Anterior view shows sites of ligation of right and left coronary arteries. Posterior view shows heart tilted upward preparatory to taking venous samples. Since the venous ligatures were necessary, the blood samples were mixtures of normal and acid blood; nevertheless, they showed pH readings as low as 6.4 (see text).

area becomes exhausted to the point of necrosis. It is apparent that in such cases the accumulation of acid metabolites in the ischemic area can well be of a magnitude to account for pain. A similar conclusion is suggested with reference to the pain in ischemic extremities, since Katz, Kerridge, and Long (1925) found that skeletal muscle becomes even more acid than cardiac muscle when stimulated to fatigue.*

DISCUSSION OF EXPERIMENTAL RESULTS WITH REFERENCE TO PAIN OCCURRING IN CLINICAL CONDITIONS

In most discussions of visceral pain the emphasis has been placed upon the sensitivity of the parietal layers of the serous membranes and upon referred pain (Head, 1893; Mackenzie, 1893). However, a number of observers (Ross, 1888; Hurst, 1911; Ryle, 1928 and 1929; Morley, 1929; Rudolf and Smith, 1930) have stressed the local or "splanchnic" pain felt in the viscus itself, and an increasing number of clinicians are coming to recognize that such pain exists and may be of aid in establishing a proper diagnosis.

By means of the method of intraarterial injection described in Part I, it has been demonstrated that pain endings are widely distributed to somatic and to visceral structures, and that the viscera possess a pain sensibility of their own which is entirely independent of the parietal peritoneum and of the body wall (Part III). By means of additional experiments (Part IV) it was possible to trace the peripheral paths of the afferent nerve fibers subserving this sensibility. They reach the viscera by accompanying the arteries. Those supplying the abdominal organs pass to the spinal cord by way of the sympathetic trunks and their splanchnic branches as shown in Fig. 2. The fibers for the thoracic viscera traverse the thoracic sympathetic trunks. In both instances the fibers enter the spinal cord by way of the rami communicantes and the posterior spinal roots. The experiments apparently exclude the vagus and phrenic nerves from any part in the supply of pain fibers to the abdominal organs. Furthermore, we have seen no indication that these nerves contribute to the pain sensibility of the heart and lungs. In view of certain referred pains it seems probable that the phrenic nerves do convey sensory fibers from the diaphragm. The diaphragm, however, is a somatic structure. From the experimental evidence we are led to conclude that the sensory innervation of the abdominal and thoracic viscera is uniformly a function of a group of posterior root fibers which reach the organs by traversing the rami communicantes and the sympathetic trunks.

*In a separate series of animals, all of the major cardiac veins were ligated to produce venous congestion. Although the heart became markedly congested and its surface "wept" copiously from transudation, the lowering of the pH of the coronary venous blood was so slight as to be questionable and there was no constant change in the lactic acid content. After twenty to thirty minutes of congestion, the heart continued to perform its function in an apparently normal manner (Moore and Greenberg, 1937).

It is our belief that this group of visceral pain fibers constitutes the peripheral conduction mechanism underlying the "splanchnic" pain of Ross and later observers. Its anatomic arrangement is consistent with the character of visceral pain. For example, the peripheral paths are entirely distinct from those of the somatic afferent fibers which supply the parietal serous membranes. This anatomic separation is in line with the functional independence of the two groups of fibers which is evidenced by clinical observation. "Splanchnic" pain is usually a nauseating pain, rather indefinitely localized in the pit of the abdomen. Apparently it signifies a disturbance within the confines of the viscus (Ryle, 1926). An illustration is the epigastric pain at the onset of appendicitis, due, according to Morley (1928), to increased intraappendicular tension. However, if inflammation develops and spreads to the parietal peritoneum, the disease syndrome undergoes a sudden transformation. The pain shifts to the right lower quadrant and immediately becomes accompanied by acute tenderness, cutaneous hyperalgesia, and reflex spasm of the overlying body wall. The sharp contrast in these two clinical pictures is readily understood in view of the complete independence of the two afferent nerve systems which are involved.

Furthermore, although the system of pain fibers supplying the viscera is a segmental system to the extent that fibers from each viscus enter the spinal cord within a certain regional zone, our experiments in abolishing visceral sensibility by posterior root section indicate that these zones are broad, the zone for each organ including a number of spinal segments. Head (1893) arrived at a similar conclusion in attempting to assign a segmental level to each viscus from his observations upon referred pain. This plurisegmental spinal representation is no doubt one reason for the diffuse nature of many "splanchnic" pains. However, in accounting for the tendency for visceral pain to be vague and poorly localized there are additional factors to note. Certain of our experiments suggest a quantitative element, since they indicate that pain fibers are less richly supplied to the internal organs than to the skin. Furthermore, in this connection it should be recalled that the ability to discriminate between stimuli applied at separate points in somatic areas is not perfect at birth. It is developed with the aid of experience and the special senses. In time it becomes quite accurate for stimuli affecting the surface of the body, especially in areas which the individual can touch and see. In contrast, the ability remains poorly developed for stimulation arising in internal organs where painful processes are infrequent and the special senses can be of little aid.

In considering the changes which may serve to produce visceral pain, certain points are frequently overlooked. It must be remembered that injury to a pain fiber at any point along its course may

give rise to painful sensation just as does stimulation of its ending. Most nerve trunks and nerve branches contain a proportion of pain fibers. When such mixed nerves are injured, the sensation of pain is aroused. It is probable that a great part of the pain incident to surgical procedures arises from such accidental traumatization of pain fibers rather than from stimulation of pain endings.

Surgeons recognize that pain may arise when a major nerve trunk is traumatized (e.g., cervical rib). Curiously enough, however, the principle is usually forgotten when the nerves concerned are small or microscopic. Consequently, there has been a tendency to consider any occurrence of pain during surgical manipulations of the viscera as evidence of a specific sensitivity supplied for the express purpose of protecting the viscus from that particular form of trauma. For example, it is a matter of common surgical experience that in operations under imperfect local anesthesia the patient is particularly apt to experience pain from manipulation about the arteries. As a result, the arteries have been assigned a sensitivity to almost every form of mechanical trauma. However, results from experimental traumatization of arteries presented in Part II suggest that this sensitivity does not reside in the vessel, but that it is a property of the mixed nerve which invariably accompanies the artery. During most surgical procedures there is gross injury to pain fibers and pain endings. For this reason observations on pain which accompanies such operations are not a proper basis for deductions regarding the origin of pain in disease.

Sensory nerve fibers as a class end in relation to some specialized terminal body or end organ. An example is the taste bud. Because of its specialized structure, it is sensitive to the chemical variations which are recognized as taste. Furthermore, it encapsulates the nerve ending and protects it from other types of stimulation. Thus, by virtue of its end organ, the taste fiber has a specific sensitivity. Similarly, many cutaneous endings have specialized receptors which render them particularly sensitive to touch, warmth, or cold. According to histologic studies, however, the pain fiber is an exception. It terminates as a bare, naked nerve ending without any specialized end structure (Ranson, 1936). Therefore its sensitivity cannot be specific, but is merely that of nerve tissue, namely, a highly developed irritability, or, in reality, a sensitivity to trauma. Every pain arises from some trauma to pain endings or to pain fibers. The injury may be mechanical, chemical, thermal, or electric, but the stimulus is always some form of trauma.

Since pain endings are stimulated by trauma, the observation that the surgeon can crush or cauterize the intestine without eliciting pain must mean that in such manipulations too few of the scattered nerve endings are injured at one time to provide a stimulation sufficient to

reach conscious levels. If a large surface of the intestine was burned at one moment, pain might well result. Certainly the localities in which abdominal pain fibers are concentrated are sensitive to heat and cauterization of a major splanchnic nerve provides a tremendous stimulus. It is a common physiologic observation that in areas of low sensibility massive stimulation may be required to elicit sensation. This is illustrated by our own experiments in which pseudaffective reactions were evoked when irritants were injected by way of the splenic artery. Although the spleen is insensitive to most manipulations, the intraarterial injections were effective, presumably because administration by way of the artery distributed the stimulus so that it acted upon a large number of receptors at one time.

Physiologically, the nerve elements supplied to the body surface constitute an exteroceptive mechanism which apprises the individual of changes in the external environment. In this somatic system lies the defense against the violence of wounds. Although the greater part of the sensitivity resides in the skin, there is certainly some protection in the deeper parietal layers where the offending instrument encounters nerve trunks and pain fibers, as well as pain endings. Once the knife has entered the peritoneal cavity, however, it may produce extensive visceral injury without eliciting pain. In general, the visceral organs are insensitive to this form of stimulation. We have suggested that this insensitivity should be attributed in part to the scattered distribution of pain fibers in visceral areas and in part to the tendency of more moderate discharges from internal organs to expend themselves upon lower centers of the nervous system without ascending to conscious levels.

We have encountered no evidence whatever of any qualitative difference between the pain endings supplied to the viscera and those supplied to the skin. However, the viscera are not normally subjected to the external stimuli which play upon the surface receptors. Visceral pain arises from changes in the internal environment and the processes of internal stimulation may differ from those for the skin. Nevertheless, in view of the nonspecific nature of the sensitivity of pain endings, the visceral stimuli, whatever their character, must act upon the nerve ending by producing a trauma. This trauma is not necessarily mechanical. It may well be chemical or physicochemical as other experiments have shown.

Among the most striking pains seen in visceral disease are those associated with mechanical disturbances in the hollow organs. Clinical evidence suggests that these pains are the result of undue tension or sudden changes in tension in the wall of the organ involved (Kuntz, 1934). Distention of an organ may give rise to continuous pain. Exaggerated contractions of its smooth muscle often give pain which

has a rhythmic character. In either instance the pain is associated with distortion. It seems reasonable that in such conditions the nerve elements can be affected mechanically. In distended organs nerve fibers could be deformed by stretching; whereas, in spastic organs the nerve elements might be actually compressed. On the contrary, however, the stimulation may be other than mechanical. When the wall of a hollow viscus is subjected to tension, its blood-vessels are proportionately collapsed. Thus, tense muscle is ischemic muscle, and our experiments have shown that in ischemic tissues definite chemical changes occur and must be considered in explaining the cause of visceral pain.

A second source of visceral pain is inflammation. It has been customary to ascribe the pain of inflammatory lesions to the mechanical effects of the swelling. There seems to be no reason to deny that the interstitial tension developed in many inflammatory swellings may act to compress and distort pain endings to the point of stimulation. However, the pain in inflammatory lesions is not always proportionate to the tumefaction or to the induration. Some stony-hard inflammations give surprisingly little discomfort and in angioneurotic edema extreme swelling may arise rapidly without producing pain. For this reason it is probable that additional factors play a part.

Our experiments demonstrate that pain endings are highly sensitive to the potassium ion (Table I). As noted in Part V, this finding is of interest with regard to pain arising in inflammations, since various observers have found the potassium content to be elevated in inflammatory fluids. It is quite possible that in inflammation various chemical changes operate to produce pain. This view is strengthened by indirect evidence that the nerve endings in inflamed areas are hypersensitive. In unpublished experiments performed in collaboration with H. Klaproth, we irradiated one lower extremity in a series of animals. After hyperemia had developed, it was found by intra-arterial injections that the pain endings of the irradiated limb were stimulated by abnormally low concentrations of an irritant; whereas, those of the untreated limb showed the same irritability as in normal animals. At present we have other experiments in progress to test the part which chemical changes may play in the production of pain in inflammation.

In our opinion the third major source of visceral pain is arterial obstruction or ischemia. During the past few years there has been a growing tendency to attribute to such pain a chemical cause. The one factor common to all ischemic conditions is deficient circulation. As a consequence, ischemic lesions uniformly represent areas in which the acid débris of anoxidative metabolism has accumulated in proportion to the degree of isolation from the arterial stream. For this

reason many writers have suggested an acid origin for pain associated with lesions of this type both in the extremities and in the heart.

In one group of experiments (Part V) we have determined the degree of acid reaction required to stimulate pain endings. In another series of animals (Part VI) we have measured the acidity of the blood from the ischemic heart. The experimental results indicate that in coronary obstruction the accumulation of acid metabolites in the area devoid of arterial circulation constitutes an adequate stimulus to arouse cardiac pain.

Pain resulting from changes arising within the body is of important service in the adjustment of the organism in health and in disease. The clinical interpretation of such pain is difficult. In many instances this is because the mechanism of pain production remains obscure. Experimental studies of the physiologic processes underlying visceral pain bear considerable promise, and attention to the part which chemical stimuli may play seems of such importance as to repay still further investigation.

SUMMARY

Injection of irritating solutions into the tissues by way of an artery serves to stimulate pain endings which are located in the vicinity of the capillary bed. Both in decerebrate and in barbitalized animals this stimulation results in characteristic reflex activity of a pseudaffective nature (Part I).

By observing the occurrence or absence of such pseudaffective reactions following intraarterial injections, results have been obtained which are of interest in connection with various problems relating to visceral pain (Parts II to VI).

The appearance of pseudaffective reactions when injections are made by way of visceral arteries demonstrates that the internal organs are sensitive to pain. Experiments show, moreover, that the vagus and phrenic nerves play no part in this sensibility. It is supplied by a group of posterior root fibers which traverse the rami communicantes and the sympathetic trunks or the splanchnic nerves. This system of pain fibers to the viscera is entirely distinct from the somatic system which subserves the sensibility of the parietal layers of the serous membranes. Apparently it constitutes the conduction mechanism underlying the local or so-called "splanchnic" form of visceral pain.

A study with reference to arterial pain sensibility is reported. It is believed that the manipulation of arteries gives rise to pain largely as a result of trauma to the accompanying gross nerve trunks.

Other observations bear upon the sensitivity of pain endings to chemical solutions and suggest that the interpretation of stimulation

in terms of cell membrane permeability may be extended to apply to the production of pain. Substances which penetrate the membrane rapidly have a marked stimulating effect. Thus, pain endings are sensitive to concentrations of potassium ion known to exist in inflammatory fluids. In contrast, magnesium salts protect the nerve membrane by a narcotic-like action which recommends their use in the clinical relief of pain.

Pain endings are found to be sensitive to a degree of acidity which is attained in ischemic tissues. Hence, the principle of acid stimulation is advanced to account for the pain arising in connection with arterial obstruction, whether skeletal or coronary. Moreover, such stimulation is possibly a factor in the production of pain in spastic organs and also in the cutaneous areas of reflex vasoconstriction which are associated with visceral disease.

The pain accompanying surgical procedures results from gross injury both to pain endings and to pain fibers. The somatic system of receptors provides the defense against this violence of wounds. In contrast, the viscera are relatively insensitive to mechanical trauma. Visceral pain is due to changes in the internal environment. Therefore, in visceral areas the processes of stimulation may differ, and the experiments indicate that chemical stimuli play an important part.

REFERENCES

Burget, G. E., and Livingston, W. K.: Pathway for Visceral Afferent Impulses From Forelimb of Dog, Am. J. Physiol. **97**: 249, 1931.

Dawson, W. T., and Bodansky, O.: Interruption of Perfusion of Isolated Rabbit Heart Upon Reaction of Coronary Flow, Proc. Soc. Exper. Biol. & Med. **28**: 635, 1931.

Häbler, C., and Hummel, R.: Über die Schmerzauslössende Wirkung des K-ions. Zugleich ein Beitrage zur physikalischen Chemie der Entzündung, Klin. Wchnschr. **7**: 2151, 1928.

Head, H.: On Disturbances of Sensation With Special Reference to the Pain of Visceral Disease, Brain **16**: 1, 1893.

Hurst, A. F.: The Goulstonian Lectures on the Alimentary Canal in Health and Disease; I., Lancet **1**: 1051, 1911; II., Lancet **1**: 1119, 1911; III., Lancet **1**: 1187, 1911.

Katz, L. N.: Mechanism of Pain Production in Angina Pectoris, Am. Heart J. **10**: 322, 1935.

Katz, L. N., Kerridge, P. T., and Long, C. N. H.: Lactic Acid in Mammalian Cardiac Muscle. Part III. Changes in Hydrogen-Ion Concentration, Proc. Roy. Soc. London **99B**: 26, 1925.

Katz, L. N., Lindner, E., and Landt, H.: On the Nature of the Substance (s) Producing Pain in Contracting Skeletal Muscle: Its Bearing on the Problems of Angina Pectoris and Intermittent Claudication, J. Clin. Investigation **14**: 807, 1935.

Keefer, C. S., and Resnik, W. H.: Angina Pectoris—a Syndrome Caused by Anoxemia of the Myocardium, Arch. Int. Med. **41**: 769, 1928.

Knapp, M. E.: The Afferent Nerve-Supply of Blood-Vessels, Minnesota Med. **12**: 759, 1929.

Kuntz, A.: The Autonomic Nervous System, Philadelphia, 1929, 1934, Lea & Febiger.

Lewis, T., Pickering, G. W., and Rothschild, P.: Observations Upon Muscular Pain in Intermittent Claudication, Heart **15**: 359, 1931.

Lillie, R. S.: Protoplasmic Action and Nervous Action, Chicago, 1923, Univ. Chicago Press.

Livingston, W.: The Clinical Aspects of Visceral Neurology, Springfield, Ill., 1935, Charles C. Thomas, Publisher.

Mackenzie, J.: Some Points Bearing on the Association of Sensory Disorders and Visceral Disease, Brain **16**: 321, 1893.

Meyerhof, O., and Lohmann, K.: Über die Vorgänge bei der Muskelermüdung, Biochem. Zeitschr. **168**: 128, 1926.

Mixter, W. J., and White, J. C.: Pain Pathways in the Sympathetic Nervous System, Arch. Neurol. & Psychiat. **25**: 986, 1931.

Moore, R. M., and Moore, R. E.: Peripheral Course of Sensory Nerves Supplying Arteries of Lower Extremity, Proc. Soc. Exper. Biol. & Med. **29**: 919, 1932.

Moore, R. M., Williams, J. H., and Singleton, A. O., Jr.: Vasoconstrictor Fibers—Peripheral Course as Revealed by a Roentgenographic Method, Arch. Surg. **26**: 308, 1933.

Moore, R. M., and Moore, R. E.: Studies on the Pain-Sensibility of Arteries. I. Some Observations on the Pain-Sensibility of Arteries, Am. J. Physiol. **104**: 259, 1933.

Moore, R. M., and Singleton, A. O., Jr.: Studies on the Pain-Sensibility of Arteries. II. Peripheral Paths of Afferent Neurones From the Arteries of the Extremities and of the Abdominal Viscera, Am. J. Physiol. **104**: 267, 1933.

Moore, R. M., and Porter, E. L.: Reactions to Irritating Arterial Injections in Decerebrate and Chronic Spinal Cats, Am. J. Physiol. **109**: 76, 1934.

Moore, R. M.: Some of the Principles Underlying the Surgery of the Visceral Nerves, Texas State J. Med. **29**: 554, 1934.

Moore, R. M., Moore, R. E., and Singleton, A. O., Jr.: Experiments on the Chemical Stimulation of Pain-Endings Associated With Small Blood-Vessels, Am. J. Physiol. **107**: 594, 1934.

Moore, R. M.: The Stimulation of Peripheral Nerve-Elements Subserving Pain-Sensibility by Intra-Arterial Injections of Neutral Solutions, Am. J. Physiol. **110**: 191, 1934.

Moore, R. M., and Singleton, A. O., Jr.: A Pseudaffective Reflex Evoked by Injections Into the Left Coronary Artery and the Peripheral Paths of the Pain-Fibers Which Are Concerned, Am. J. Physiol. **113**: 99, 1935.

Moore, R. M., and Singleton, A. O., Jr.: Peripheral Course of Pain-Fibers Supplying Coronary Arteries and the Myocardium, Proc. Soc. Exper. Biol. & Med. **32**: 1492, 1935.

Moore, R. M., and Greenberg, M. M.: Acid Production in the Functioning Heart Under Conditions of Ischemia and of Congestion, Am. J. Physiol. **118**: 217, 1937.

Morley, J.: Abdominal Pain as Exemplified in Acute Appendicitis, Brit. M. J. **1**: 886, 1928; The Significance of the Afferent Impulses From the Skin in the Mechanism of Abdominal Pain, Lancet **2**: 1240, 1929.

Odermatt, W.: Die Schmerzempfindlichkeit der Blutgefässe und die Gefässereflexe, Bruns' Beitrage z. klin. Chir. **127**: 1, 1922.

Ranson, S. W.: The Anatomy of the Nervous System, Philadelphia, 1936, W. B. Saunders Co., page 68.

Reimers, C.: Über die Wirkung der Incision auf das physikalischchemisch Bild der Entzündung, Deutsch. Zeitsch. f. Chir. **236**: 60, 1932.

Ross, J.: On the Segmental Distribution of Sensory Disorders, Brain **10**: 333, 1888.

Rudolf, R. D., and Smith, A. G.: Observations on Visceral Pain, Am. J. M. Sc. **180**: 558, 1930.

Ryle, J. A.: Visceral Pain and Referred Pain, Lancet **1**: 895, 1926; The Clinical Study of Pain: With Special Reference to the Pains of Visceral Disease, Brit. M. J. **1**: 537, 1928; Abdominal Pain: III. Observations on Colonic Pain, Guy's Hosp. Reports **79**: 395, 1929.

Stöhr, P., Jr.: Mikroskopische Anatomie des Vegetativen Nervensystems, Berlin, 1928, Julius Springer, page 84.

Walton, F. E., Moore, R. M., and Graham, E. A.: The Nerve Pathways in the Vomiting of Peritonitis, Arch. Surg. **22**: 820, 1931.

White, J. C.: The Autonomic Nervous System, New York, 1935, The Macmillan Company.

Woodworth, R. S., and Sherrington, C. S.: A Pseud-Affective Reflex and Its Spinal Path, J. Physiol. **31**: 234, 1904.

Woollard, H. H.: The Innervation of Blood Vessels, Heart **13**: 319, 1926.

CARCINOMA OF JEJUNUM

Report of a Case

Howard M. Kern, M.D., Baltimore, Md.

(From the Department of Surgery, Sinai Hospital)

C. E. B., male, aged fifty-four years, a steel worker, was referred to me and admitted to the Sinai Hospital August 5, 1935. There was nothing in the past history of any significance except a story of constipation for twelve years. The patient's chief complaint was pain in the stomach.

The present illness was of approximately one year's duration, when the patient began to have periodic attacks of excruciating pain in the abdomen which usually started in the right lower quadrant and radiated to the left. In the beginning the attacks were rather infrequent and lasted but a few seconds; they were unaccompanied by nausea or vomiting and were relieved by a bowel movement. Medical aid was sought and the patient was treated for indigestion and constipation by his physician. He was able to continue his work and "felt pretty good when his bowels were not tied up." Seven weeks prior to his hospital admission, the attacks of abdominal pain became more frequent, of greater intensity and longer duration. He consulted another physician who had x-ray studies of the gastrointestinal tract made. The radiologist reported as follows: "Film shows immediately after administration of barium, the stomach, duodenum, and jejunum markedly dilated, but at the end of six hours the barium meal is in the terminal ileum. The large intestine is spastic." (Fig. 1.)

Tincture of belladonna, drops 10, after each meal was given with no relief of symptoms. There was a gradual loss of appetite and weight; stools became infrequent in spite of catharsis and enemas. The patient became progressively worse. There was no bowel movement for sixteen days. Six days prior to admission to the hospital, vomiting began and recurred at frequent intervals. Blood was never seen in the vomitus or stool.

Physical Exam.—The patient is a well-developed man who had evidently lost considerable weight. The skin was dry and the mucous membranes pale. An occasional râle is heard in the chest.

On inspection the abdomen was full and active peristaltic patterns were visible in the left upper quadrant. On palpation there is right-sided muscle spasm and tenderness, particularly in the region of the gallbladder. The liver edge could be felt two fingers' breadth below the costal margin in the midclavicular line and was sharp and nodular. No masses were felt elsewhere. On auscultation marked gurgling was heard everywhere.

Rectal Exam.—Palpation and proctoscopic examination failed to reveal any abnormality.

Laboratory Exam.—Urine gross and microscopic negative. Stool positive for occult blood. Blood: hemoglobin, 70 per cent; R.B.C., 5,000,000 per cu.mm. (probably due to concentration); leucocytes, 8,000 per cu. mm.; differential normal. Blood chemistry: urea N., 17.36; urea, 37.15; sugar, 0.077; Wassermann, negative. Phenolsulphonpthalein, 40 per cent in two hours.

Course in the Hospital.—It was our impression that the patient was suffering from a low incomplete intestinal obstruction, probably due to a malignant growth in the colon. The gastrointestinal x-rays taken six weeks previously were reviewed, but no

Received for publication, November 5, 1937.

filling defect could be found. The day following admission to the hospital a barium enema was given, and the x-ray report was as follows: Spastic colon, no dilatation or filling defect.

The following note was made by the interne: After the x-ray examination of the large intestine, the patient experienced severe cramps, had two bowel movements, and vomited three times. The vomitus was copious and bile stained.

Fig. 1.—X-ray taken shortly after the administration of barium, showing the marked dilatation of stomach, duodenum, and jejunum.

The abdomen now appears to be divided into two parts by a line drawn through the umbilicus. The right side is spastic, the upper quadrant appears full. Every five or ten minutes simultaneously with cramp-like pains a mass appears in the right lower quadrant gradually increasing in size and disappearing in a like manner.

Glucose and normal salt were administered intravenously. General effectual cleansing enemas were given to remove the barium, and an exploratory laparotomy was performed on August 6 about forty-eight hours after admission to the hospital.

Operation.—The operation was begun under spinal anesthesia which unfortunately was incomplete and was supplemented by gas and ether. Through a midright rectus incision, the cecum, ascending and transverse colon, stomach, and liver were palpated and found to be normal. Just below the stomach a hard mass was palpated and delivered through the incision. It proved to be a growth completely encircling the jejunum, just about 17 cm. from the duodenal jejunal flexure. It was of stony hardness, about 3 cm. long, and seemed to constrict the gut to a point of complete occlusion. The proximal jejunum was dilated to about twice its normal size, the wall greatly thickened and edematous. The stomach and duodenum were also dilated. The mesentery in the region of the growth was occupied by a large mass of stony hard glands which extended to the spine. On the serosa of the jejunum below the growth were numerous scattered pea-sized nodules which were taken to be metastatic growths.

Resection seemed unjustifiable so a lateral anastomosis of jejunum to jejunum short circuiting the growth was performed. Anastomosis and closure of abdomen performed in the usual manner.

Postoperative Course.—The patient developed bronchopneumonia twenty-four hours later and died on the fifth day postoperative.

PARTIAL AUTOPSY (SMALL INTESTINE ONLY)

External Appearance.—The body was that of a well-developed, well-nourished white male of fifty-four years of age; weight, about 150 pounds; height, 167 cm. There was no rigor mortis, no edema, and some postmortem lividity of dependent parts.

Face.—The face was full and well nourished. Pupils were equal.

Skin.—There were a few needle sticks in antecubital fossae. The midrectus incision, 10.5 cm. in length, was healing nicely. Skin edges were sutured with interrupted black silk sutures and two interrupted silver wire stay sutures.

Abdominal Walls.—Incision was noted as above. Fascia and muscle were sutured with catgut. Below and in the lower part of the rectus there was a pocket of thick gelatinous serum which extends directly onto a few loops of small bowel for the peritoneum was deficient just under the center of the incision.

Abdominal Cavity.—A very small amount of slightly turbid fluid was present in the paracecal gutter. Just under the incision, a few loops of small bowel were enormously distended, so much so that definite striae appeared (lending a faint suggestion of taenia). This section of gut, when traced just across the midline to the left, ended in a complete U-shaped lateral anastomosis. The anastomosis was about 17 cm. past the end of the duodenum. The parietal peritoneum surface was smooth and glistening. There was no injection present. There were a few scattered white firm nodules present, situated on the peritoneum of the small bowel, particularly the jejunum and one on the sigmoid colon. The mesentery of the jejunum contained many large and small hard masses. The omentum was small and adherent laterally on both sides, but it was not adherent to or even in the neighborhood of the anastomosis. The liver was not enlarged and there were no visible metastases. The kidneys and spleen were normal to palpation. The bladder was dilated. The para-aortic nodes were enlarged.

Intestines.—Serosa of the small intestine contained scattered, white nodules (1 to 2 mm. in diameter). The duodenum and first 17 cm. of the jejunum were quite dilated and brought on the appearance of taenia. At this point (17 cm.) there was a lateral anastomosis which was formed by a doubling back of the jejunum on itself. At the U-shaped anastomosis there was a firm, hard, rounded mass 3 cm. in diameter which occupied the entire lumen and was part of the wall itself on all sides. The tumor mass apparently encircled and narrowed the total diameter of the bowel above

and below this point. For about 8 cm. above and below the mass, the bowel was sutured together and slightly injected. There was excellent peritonealization. There was no exudative process and no leaking. The ostium measured 6 cm. across and water flowed very easily through it from the proximal out through the distal portion. When the bowel was opened along the lateral margins, the tumor stood out as a hard, firm encircling mass, ½ inch wide, which encircled and almost occluded the bowel. The intestinal surface was apparently eroded and the tumor extended through the muscularis to the peritoneal surface. It appeared limited to ½ inch. Above the obstruction, the bowel was dilated, measuring 10 cm. in diameter, and the valvula conniventes stood out as ridges. No other ulcerative areas were noted. The small pea-like areas were not particularly suggestive of metastases when sectioned.

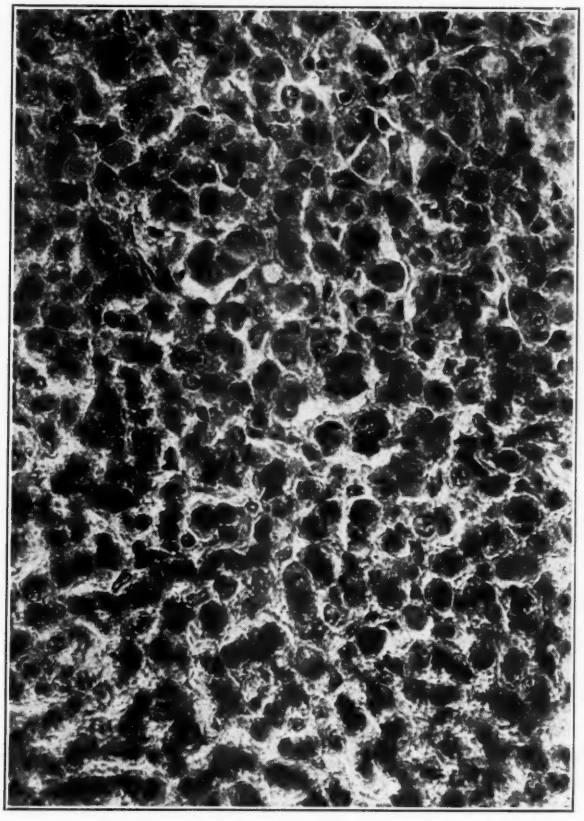


Fig. 2.—Photomicrograph of a section through the tumor, showing round and cuboidal cancer cells. The cytoplasm is granular. The large oval nuclei with frequent mitotic figures and many hyperchromatic particles are pushed toward the periphery.

Provisional Anatomical Diagnosis.—

1. Bronchopneumonia—bilateral (history).
2. Annular carcinoma of jejunum.
3. Metastases to small and large bowel and to mesentery and para-aortic nodes.
4. Postoperative, lateral anastomosis of jejunum.

MICROSCOPIC NOTES

Jejunum.—Section was distorted. Serosa was present only in a few places and there were no signs of metastatic cells. Circular and longitudinal muscle layers were

normal, as also were submucosa and crypts of lieberkuhn and lining epithelium. There were no metastases.

Tumor.—A small portion of normal jejunal mucosa stood out, limited on one side by the cut of the section, fading out insensibly into a distinct carcinomatous invasion. The latter was most marked and ran wild in the submucosa and invaded and eliminated the circular layer of muscle, while many malignant cells were found scattered through the longitudinal layer. The native of the tumor was most clear in the muscularis area. Here and there were numerous small glandular-like nests of cells. The cells were cuboidal and round in shape. The cytoplasm stained pale pink and was granular; and the large oval nucleus with frequent mitotic figures and many hyperchromatic particles were pushed toward the periphery. There were also large round cells filled for the most part with a large clear staining drop of fluid which forced the nucleus toward the outer edge of the cell and elongated its contour producing a typical signet cell (Fig. 2). The distribution of the tumor cells was irregular—now densely packed, now quite loose, and again in long strands of double thickness.

Mesentery and Mesenteric Lymph Nodes.—

1. Mesentery was free of metastases.

2. Lymph nodes showed some activity of mononuclear cells in areas scattered through the node.

Another mesenteric node showed profuse metastatic infiltration which consisted of many small islets of cells which looked quite glandular and which distorted the structure of the lymph node completely. The cells were the same as those described with the tumor except that colloid degeneration had not occurred.

Pre-Aortic Lymph Node.—No pathology.

Jejunum with Metastasis to Serosa.—No deposits of malignant cells were made out.

FINAL DIAGNOSIS

1. Annular adenocarcinoma of jejunum with colloid degeneration and metastases to mesenteric lymph node.

2. Postoperative lateral anastomosis to jejunum.

3. Bronchopneumonia—type undetermined (history).

Cause of Death.—Incomplete postmortem examination.

INCIDENCE

According to most references, primary adenocarcinoma of the jejunum is extremely rare, and up to the present writing but 83 verified examples of this type of tumor have been operated upon. Undoubtedly, other cases have occurred but they have not been reported in the literature.

In 1922 Johnson[1] reviewed a series of 41,883 autopsies from the Vienna General Hospital. In this series were 343 cases of intestinal carcinoma, but not 1 case of carcinoma of the jejunum. Rankin and Mayo[2] on the other hand reported an incidence of 0.062 per cent of all carcinoma of the intestinal tract in the small intestine and stated that they found the jejunum to be the most common site. Barron[3] stated that 8 per cent of all carcinomas appear in the gastro-intestinal tract; 4 per cent of this number occur in the small intestine; the most common site is in the duodenum next to the ileum and rarely in the jejunum. Newton and Buckley[4] gathered reports from European

clinics and departments of pathology of eight of the largest hospitals in this country and found only 23 verified cases among 135,000 necropsies.

An analysis of the reported cases reveals that men are affected about twice as frequently as women and that the decade of greatest incidence is from thirty to forty years of age.

SYMPTOMATOLOGY

There is no characteristic symptomatology of carcinoma of the jejunum; and after a careful perusal of the literature we find that very few cases were diagnosed before operation, and in many cases the growth was found at autopsy. The disease is usually insidious and may be present for many months before the patient seeks medical relief when the *subjective* symptoms of chronic partial obstruction begin.

My own case is typical, with a history of indigestion, constipation, and attacks of sharp upper abdominal pain simulating gallbladder colic. Vomiting begins later in the disease and usually comes on shortly after the taking of food as the growth is usually high in the jejunum. The vomitus is copious, contains bile, and has no fecal odor. There has been no recorded instance of blood in the vomitus; however, occult blood is found in the feces when the growth becomes ulcerated. The stage or degree of obstruction determines the clinical picture of the disease. Perforation into the general peritoneal cavity with localized or generalized peritonitis has been reported and also intussusception of the growth into jejunum.

Several of the reported cases were originally diagnosed as pernicious anemia, the main symptoms being fatigability, gastric distress (due to absence of hydrochloric acid), and later progressive loss of weight.

DIAGNOSIS

In spite of all laboratory tests and x-ray examinations it is extremely difficult in most cases to make a correct preoperative diagnosis. On account of the rarity of occurrence, cancer of the small bowel is seldom considered in making a differential diagnosis of abdominal disease; however, it should always be considered in the presence of upper abdominal colic with vomiting.

Gabor and Heller[5] emphasize the importance of x-ray studies in determining the presence, then the localization, of the growth and they state that any delay in the emptying time of the small intestine beyond eight hours must arouse suspicion as to the presence of a growth. They recommend that x-ray plates be taken at short intervals following the administration of the contrast medium, thereby enabling one to catch the point at which blockage is occurring. On account of the rapid emptying of the small intestine one does not usually get the characteristic filling defect caused by growths in the large gut.

Blood may or may not be found in the stools, depending upon whether or not the growth is ulcerated. Its presence otherwise unexplained is significant.[6]

TREATMENT AND PROGNOSIS

Obviously resection and anastomosis is the operation to be performed when the growth is removable, however, the great majority of cases come to exploration at a time when such a procedure is neither possible nor justifiable. Therefore, the operation is usually one aimed simply at relief of the obstruction. The malignancies of this part of the intestinal tract are of a very high degree, and in the Rankin-Mayo[7] series of 55 cases it was concluded that the "prognosis in carcinoma of the small bowel whether the growth is apparently satisfactory for resection or whether the operation is palliative," is unsatisfactory. No patient in their series lived longer than three years, even when radical resection of the growth had been performed.

SUMMARY

A case of primary carcinoma of jejunum with colloid degeneration is reported.

The diagnosis is exceedingly difficult to make early in the disease. There is no characteristic symptomatology and the greatest help is obtained from x-ray studies.

The prognosis is very poor on account of the high degree of malignancy of tumors of the small intestine, even in those cases that can be resected.

REFERENCES

1. Johnson, R.: Carcinoma of the Jejunum and Ileum, Brit. J. Surg. **9**: 422, 1922.
2. Rankin, F. W., and Mayo, C. W.: S. Clin. North America **12**: 915-917, 1932.
3. Barron, M.: Abstract of Discussion on Intestinal Carcinoma, J. A. M. A. **92**: 287-291, 1929.
4. Newton, F. C., and Buckley, R. C.: Primary Adenocarcinoma of Jejunum with Report of Two Cases, New England J. Med. **202**: 255-261, 1930.
5. Gabor, M. E., and Heller, R. I.: Primary Carcinoma of Jejunum, Am. J. Surg. **27**: 120-125, 1935.
6. Harris, F. I., and Rosenbloom, H.: Primary Carcinoma of Jejunum, Arch. Surg. **23**: 805-812, 1931.
7. Rankin, F. W., and Mayo Clinics: Carcinoma of the Small Bowel, Surg. Gynec. & Obst. **50**: 939-947, 1930.

MECKEL'S DIVERTICULUM

A Review of Twenty Cases With Report of Two Cases

John deJ. Pemberton, M.D., and Leonard K. Stalker, M.D.,*
Rochester, Minn.

(From the Division of Surgery of the Mayo Clinic and the Mayo Foundation)

MECKEL'S diverticulum is a developmental anomaly of the intestinal tract which affects about 2 per cent of the population, with males predominating in a ratio of 2:1. The majority of persons who have the anomaly undoubtedly go through life without symptoms from it. There occurs, however, in approximately one-fourth of all cases of Meckel's diverticulum, some pathologic change, such as an inflammatory process, a mechanical disturbance, development of heterotopic tissue, or development of a tumor.

A review of 20 consecutive cases of Meckel's diverticulum encountered at operation by one of us indicates that, in general, such cases can be classified in three groups; namely, those which present the following: (1) no symptoms, (2) symptoms of intestinal obstruction, and (3) symptoms of intestinal bleeding. Eight of the 20 patients had symptoms owing to the presence of the diverticulum and were relieved following operation. The diverticulum in the remaining 12 instances was found at the time laparotomy was performed for another condition. It seemed advisable, in 6 of these 12 cases, to remove the diverticulum as a prophylactic measure. Removal of the diverticulum was considered unnecessary in the other 6 cases. There was no mortality in the 14 instances in which the diverticulum was removed. Of the 8 patients who had symptoms, 4 had some degree of intestinal obstruction and 4 had experienced intestinal bleeding previously. The diagnosis was made before operation in only 2 cases. Two patients recently were operated on, one of whom presented symptoms of obstruction and the other of hemorrhage; these cases seem to be worth reporting.

REPORT OF CASES

Case 1.—An obese man, aged forty-eight years, came to the Mayo Clinic for the first time in 1924 because of dyspepsia of a type usually associated with the presence of a peptic ulcer. The dyspepsia had been present for six years. In addition he had experienced for the two weeks prior to admission a bloating, gnawing sensation throughout the middle of the abdomen. This sensation was concentrated mostly in the region of the umbilicus. It was relieved by taking soda and food. Results of analysis of the gastric content and of two roentgenographic examinations of the stomach and duodenum were considered normal. A diagnosis of duodenal ulcer was

*Fellow in Surgery, the Mayo Foundation.
Received for publication, January 4, 1938.

made and the patient was dismissed to follow a reduction type of diet. A few mild symptoms occurred intermittently during the next two years and then the man experienced complete relief for ten years.

The patient returned to the clinic in August, 1936, complaining that for three months there had been slowing of his usual bowel habit, which had been associated during the last month with considerable gaseous dyspepsia and with lower abdominal cramps. These cramps were confined mostly to the lower left quadrant of the abdomen and occurred at any time of day or night, frequently awakening him. They were most marked after eating and, as a result, he took liquids chiefly. No relief was obtained by taking alkalies, but some relief could be obtained from use of enemas or by strong purgation. One week before his return to the clinic he had been given barium for a roentgenologic examination. The cramps became more severe; there was much nausea, vomiting and some increase of temperature and of pulse rate, but no bowel movements or passage of flatus occurred. This obstruction was relieved spontaneously in twenty-four hours and two days later he came to us for examination.

At this time, although it was thought that he must have had an intestinal obstruction, we could not demonstrate its site. Proctoscopic examination, repeated examinations of the feces, blood, and urine, and roentgenoscopic examination of the chest, of the abdomen, and of the portion of colon distal to the cecum were reported as having given negative results.

The patient was advised to have an abdominal exploration performed, but after several days of conservative treatment the symptoms subsided completely and he left the hospital. One week later he returned complaining of the same symptoms, but to a lesser degree than previously. Roentgenographic examination of the stomach and of the small bowel was made and gave evidence of the presence of a duodenal ulcer, marked deformity of the duodenum, and a carcinoma involving the ileum apparently within 30 inches (76 cm.) of the ileocecal valve. Considerable intestinal obstruction was present.

After preparation had been made, an abdominal exploration was performed through a right rectus incision. This revealed an obstructing lesion of the ileum about 3 to 4 feet (91 to 121 cm.) from the ileocecal valve, huge dilatation of the bowel proximal to it, and collapse of the bowel distal to it. One could not be certain of the character of the obstruction, but it seemed to be a narrow, napkin-ring tumor which involved the ileum with much inflammatory reaction surrounding it. Primary resection could not be done because of the marked obstruction. Consequently ileo-ileostomy was performed, making a lateral anastomosis between two loops of bowel, one loop 1 foot (30 cm.) proximal to, and the other 1 foot distal to, the tumor. The upper part of the abdomen was explored and no evidence of disease was found except a somewhat distended gallbladder.

The patient had an uneventful convalescence and was dismissed from the hospital on the thirteenth postoperative day. Following this operation, his symptoms ceased and he gained weight.

In November, 1936, twenty-five days later, reëxploration was performed through a right rectus incision which was made to the outer side of the previous incision. The inflammatory process had markedly subsided. The huge dilated portion of bowel previously observed was still somewhat dilated. Attached at right angles to this loop was a Meckel's diverticulum, which was 1½ inch (approximately 3.5 cm.) in diameter at its base and about 3 inches (approximately 7.5 cm.) long. The fundus was adherent posteriorly to the mesentery of the bowel and also to the loop of bowel. The diverticulum was freed and was removed and the stump was inverted by use of three rows of chromic catgut and one row of silk.

The pathologist reported the presence of a Meckel's diverticulum with linear and circular ulcers; the largest was 8 mm. in diameter and the smallest was 6 mm. in diameter. Marked regional diverticulitis was present.

The patient made an uneventful recovery and was dismissed from the hospital on the eleventh postoperative day. Since that time he has been entirely free from symptoms.

CASE 2.—A man, aged nineteen years, came to the clinic October 14, 1937, because of anemia, the cause of which, up to that time, had not been determined. Seven years previously he had become weak and very anemic; this had necessitated rest in bed for six weeks. One year later he again had become anemic. Since that time he said he had received antianemic therapy, such as liver extract and iron, constantly. Three years before he came to the clinic he had expelled several tarry stools and again had become so anemic that he had required prolonged rest in bed. Thereafter the presence of occult blood in his stools had been constant while following a meat-free diet. Severe melena had occurred again in June, 1936, and at that time the diagnosis of a bleeding duodenal ulcer was made. A rigid diet, powders, and parenteral injections of a preparation of histidine had been prescribed. No benefit was obtained from the treatment and, because of the presence of a palpable spleen, anemia, and recurrent hemorrhages, a diagnosis of splenic anemia, probably with esophageal varices, was made by another physician. The possibility of performing splenectomy was suggested to the patient and, because of this suggestion, he came to the clinic.

The man appeared anemic. The spleen was somewhat enlarged and was easily palpated. Roentgenoscopic examination of the esophagus, stomach, small intestine, and colon gave negative findings. Repeated examinations of the stool for the presence of occult blood gave positive findings and the gastric contents appeared normal. On test of hepatic function bromsulphalein was not retained. The concentration of serum bilirubin was 1 mg. per 100 c.c. of blood and the van den Bergh reaction was indirect. The value for hemoglobin was 7 gm. per 100 c.c. of blood, or 46 per cent of normal. Erythrocytes numbered 4,330,000 and leucocytes 5,300 per cubic millimeter of blood; 2.5 per cent of the erythrocytes were reticulated. Examination of the blood smear gave evidence of hypochromic anemia of marked degree and the number of platelets was increased.

A probable diagnosis of bleeding ulcer in a Meckel's diverticulum was made by the process of exclusion and exploration was advised. The exploration revealed a large and distended Meckel's diverticulum about 3 feet (91 cm.) from the ileocecal valve. At the base of the diverticulum and involving the wall of the ileum was a linear ulcer about 3 cm. in diameter. Considerable scarring, redness, and some edema were present. It was necessary to resect the small bowel in order to remove the ulcer. This was done by using a three-bladed clamp and by performing end-to-end anastomosis. Ileo-ileostomy was performed about 8 inches (20 cm.) from the anastomosis to relieve possible tension on the suture line. The appendix was not diseased and was not removed. The spleen was three times the normal size but was normal in consistency. The pathologist reported that examination of the resected bowel disclosed a Meckel's diverticulum 2.5 cm. in depth with an opening 2 cm. in diameter. A chronic ulcer measuring 3 cm. by 8 mm. by 2 mm. was present at the base of the diverticulum; also some peridiverticulitis was present.

The patient had an uneventful convalescence except for development of left femoral thrombophlebitis which became apparent on the ninth postoperative day. At the time of his dismissal from the hospital, on the twenty-seventh postoperative day, the spleen was not palpable; examinations of stool for occult blood gave negative results; the concentration of hemoglobin was 13.6 gm. per 100 c.c. of blood, or 90 per cent of normal; and the erythrocytes numbered 4,400,000 per cubic millimeter of blood.

COMMENT

The difficulty of making a diagnosis of Meckel's diverticulum and two of the common methods by which these diverticula manifest themselves are illustrated by the cases reported. The symptoms presented in both cases were originally interpreted as those of peptic ulcer. It is not unusual for a patient who has a diseased Meckel's diverticulum to receive treatment for other conditions; such as, appendicitis, cholecystitis, peptic ulcer, splenic anemia, pancreatitis, adhesions, colitis, or enteritis. Four of the eight patients who presented symptoms owing to the presence of the diverticulum had been operated on previously and the true cause of the symptoms was not recognized. One patient who had midabdominal cramps and intestinal bleeding had been subjected to laparotomy three times before the diverticulum was removed. Appendectomy had been performed at the time of the first operation and the second operation had consisted of an exploration on account of formation of adhesions. Of the other cases, appendectomy had been performed in one, cholecystectomy in another, and splenectomy and appendectomy in a third. The symptoms had not been relieved in any of these instances until the Meckel's diverticulum was removed.

It is then apparent that a positive diagnosis of diseased Meckel's diverticulum can be made with exceeding difficulty. On the other hand, such a condition frequently can be suspected and can be suggested as a probable diagnosis on the basis of exclusion of other possibilities. Diagnosis of intestinal obstruction, either complete or partial, usually is not difficult to make. In those cases in which the cause of obstruction is not apparent, the possibility of the presence of a diseased Meckel's diverticulum should be considered. The presence of unexplained secondary anemia, either with the history of intestinal bleeding or with that of melena and the presence of negative findings on roentgenographic examination of the esophagus, stomach, and colon, should make one suspect that an ulcer exists in or near a Meckel's diverticulum. Occasionally roentgenographic examination of the small bowel will demonstrate the presence of the diverticulum; this occurred in two of our cases. In a review of the roentgenograms of the small bowel in the first case, confirmation of the finding of a Meckel's diverticulum at the time of operation could be made at the present time. Diseased Meckel's diverticula occur in the majority of cases among males aged twenty years or younger, but cases have been found at all ages and they occur frequently among females.

The previous diagnosis of splenic anemia and the presence of splenomegaly in the second case and the performance of splenectomy in one of our other cases are worthy of comment. It is true that splenic anemia must be considered in the differential diagnosis if marked, unexplained anemia and splenomegaly exist. However, absence of the blood picture typical of splenic anemia, a normal finding by means of the liver func-

tion test, and absence of bleeding esophageal varices to account for the blood in the stool help to exclude this diagnosis. Splenomegaly is not, as a rule, associated with true secondary anemia, but experimentally it has been shown that chronic loss of blood from the gastrointestinal tract will produce splenomegaly. It is probable that the splenomegaly present in our cases was due to the chronic loss of blood. This conception is somewhat confirmed by the fact that the spleen decreased in size and was not palpable following operation.

We believe that the possibility of the presence of a diseased Meckel's diverticulum must be considered in differential diagnosis in all instances in which pathologic change is sufficient to explain any vague abdominal symptoms, or in which the cause of intestinal bleeding is not apparent at the time that laparotomy is performed; and, in these instances, the first 5 feet (152 cm.) of ileum should be explored for the presence of a diverticulum. A routine examination for the presence of a Meckel's diverticulum should be made in the majority of uncomplicated cases in which abdominal operation is performed; especially is this so in cases representing the younger age group and in the case in which simple appendectomy is performed. If a Meckel's diverticulum is found, it need not be removed as a routine procedure. The diverticulum should be removed as a prophylactic measure in those cases in which it has a narrow base, is long, adherent, gives any evidence of inflammation, or if it appears that possibly it might be a factor in an intestinal obstruction. A short diverticulum with a broad base which can be considered almost as an outpouching of the bowel usually can be left in place with safety, but a record of its presence should be made.

SUMMARY

Cases of Meckel's diverticulum can be classified in three groups; namely, (1) cases in which no symptoms or signs are present; (2) cases in which there are symptoms or signs of intestinal obstruction and (3) cases in which symptoms and signs of intestinal bleeding are present. Diagnosis and treatment in any case depend on the group to which the case belongs.

REFERENCE

1. Lang, F. J.: Myeloid metaplasia, Folia haemat. **43**: 95-120, 1930.

THE IMPORTANCE OF HEMATEMESIS ACCOMPANIED BY PYLORIC OBSTRUCTION

ANTHONY BASSLER, M.D., NEW YORK, N. Y.

TRIVIAL bleeding, usually from an ulcer, is a common condition and may be considered as part of a repair process. More distinct interrupted hemorrhage may exist, and it is also nonfatal. Predicated upon these and favorable results from the medical handling of more pronounced bleeding, the belief exists that hemorrhages from peptic ulcers are rarely fatal.

Tage Christiansen[1] in 289 cases of massive hemorrhage due to peptic ulcer had a 7.9 per cent mortality, with a higher percentage for women than for men. He drew attention to the fact that in late years, even with transfusions and better methods of handling, the mortality was doubled. De la Viesca[2] in 130 cases stated that hematemesis was due to gastroduodenal ulcer in 73.5 per cent; to carcinoma, in 13.6 per cent; and to gastritis, in 10.2 per cent. Repeated hemorrhages in ulcers occurred in 8.4 per cent, and 27.2 per cent of these patients died. To illustrate the opposite in reported statistics: Meulengracht[3] states his mortality to be but 1 per cent, a result, in my opinion, not possible in statistics made up on massive hemorrhage cases. In an attempt to separate the cases into the surgical and medical, Hinton[4] divided the cases into five groups and Westermann[5] stated that 10 out of 50 patients with gastroduodenal ulcer complicated by hemorrhage died in hospitals under rigid medical treatment. Goldman[6] stated that in 349 cases which entered the hospital because of gross hemorrhage or which developed this complication during the period of hospitalization 39, or 11.1 per cent, died of exsanguination; while an additional 17, or 4.9 per cent, died of conditions associated with bleeding, such as perforation, pneumonia, and cerebral or cardiac thrombosis, the total mortality being 15 per cent.

As seen in private, or office, practice, the case of peptic ulcer in which bleeding exists shows this as occult blood in the stool or rare tarry stools. A massive hemorrhage in the past history of the patient may be stated. In hospital practice, especially where an active ambulance service exists, not a few of the hematemesis cases are of the much more dramatic type, consisting of the vomiting of bright red or dark blood or the presence of marked tarry stools and a secondary anemia sufficient to produce weakness, pallor, dyspnea, and rapid thin pulse. Occasionally such a case may be seen in private homes. In the records of hospitals of our largest cities, especially those which have

Received for publication, December 29, 1937.

open ambulance services, the instances of death due to exsanguination from peptic ulcer run variously between 10 and 27 per cent, and, if conditions associated with the bleeding are considered, such as perforation, pneumonia, and cerebral and cardiac thrombosis, the percentage is nearer to the high figure than the low. Hospital records show that the rate of this mortality is varied according to age; in the young up to twenty-five years of age it is about 3 per cent, rising in almost a straight line to 42 per cent in those seventy years and over. Very probably this is due to more major pathology in older individuals and according to the condition of the local arteries (sclerosis), the amount of granulation and scar tissue in the ulcer, lesions in the posterior wall of the first and second part of the duodenum and near the lesser curvature of the stomach being conspicuous. But these figures of deaths brought about by hemorrhage are not conclusive so far as ulcer is concerned, because gastric carcinoma, hepatic cirrhosis, ruptured varicosities, splenic conditions, and gastrointestinal hemorrhage due to uremic states obscure them.

Sudden death in massive hemorrhage from the stomach or duodenum is rare, the vast majority of patients with this complication living up to two weeks. Nothing is more doubtful and often less satisfactory than continuing medical treatment day after day in the presence of continued hemorrhage, falling erythrocyte count, and lowering hemoglobin, especially when blood transfusions are not beneficial. To help in the better understanding and the redemption of some of these patients, I desire to draw attention to a small group of the whole in which, in my opinion, prompt surgery should be the therapy of choice. This article presents the significance of the combination of massive hemorrhage and pyloric obstruction from whatever cause as having a higher mortality than any other. In the control of massive hemorrhage from the stomach or duodenum stomach tonus is the main essential to control the bleeding. In pyloric obstruction the stomach is dilated and the tonus deficient. Inability of the organ to empty in normal time, with consequent accumulation of foods and fluids, causes not only a myasthenia of the muscle fibers but actually a thinning and stretching of them. This involves the circular and longitudinal fibers and eventually the organ becomes globular in shape, increases in size, and becomes deficient in ability of peristalses to empty it and practically an atonic viscus. In the observation of some of these cases there is the suggestion that associated with massive hemorrhage there is a shocked condition which expresses itself in further gastric atony.

Eight years ago there was an office case of pyloric obstruction due to ulcer, which, three days after being seen for the first time, had a gross hemorrhage and continued to vomit blood for two days. The patient lived out of New York City, was hospitalized in his home town, and because of the pyloric obstruction had an immediate gastro-

enterostomy done, upon which the hemorrhage ceased immediately and he made a prompt recovery. Since that time there have been 14 additional cases of the combination of massive hemorrhage and pyloric obstruction and the contrast of this group, all of which at the time had a gastroenterostomy without other surgery, with former cases makes them seem worthy of reporting. In these 15 cases ulcer had been previously diagnosed in 5 and carcinoma in 2, and in but 2 cases was pyloric obstruction known to be present. In 8 there had been no previous diagnosis made. In 6 of these there was a history of a gastric type of indigestion of a continued type. Eleven of them had been brought to the hospital by ambulance, 4 being seen in consultation practice and immediately hospitalized. Each case was an instance of continued bleeding after the initial vomiting of blood, due, I believe, to the presence of a pyloric obstruction of sufficient degree to render the stomach unable to contract, and where, because of the inability of the stomach to contract, gastric distention continued to keep the bleeding vessels open. It is interesting to note that in 3 of the ulcer cases the ulcer was in the duodenum, and it is difficult to understand how blood could pass a pyloric obstruction from the duodenal side into the stomach. One would assume that in an eroded vessel in the duodenum continued open from an inflammatory process with adhesions to the periduodenal structures, especially the large artery which contacts the pancreas and which artery is generally sclerosed and imbedded in inflammatory and scar tissue, there would be melena and not hematemesis. In duodenal ulcer without pyloric obstruction melena is the rule, but it seems to be a clinical fact that a duodenal ulcer, even with pyloric obstruction, may bleed actively into the stomach. How or why I do not know. Of these 15 cases, 4 recovered from the hemorrhage; 1 died of pneumonia two weeks after the operation; 1, of cardiac thrombosis on the fifth day; and 1, of exsanguination. The matter of subsequent operations is not included, this article simply presenting the suggestion of prompt gastroenterostomy in marked, continued hemorrhage into the stomach when pyloric obstruction is present. These drainage operations seem to accomplish something in the way of establishing tonus which the use of gastric tube drainage does not. In 1 of the 15 bleeding cases bleeding continued after the operation; in this, pyloric adenocarcinoma existed. In 3 more it took up to sixty hours to stop bleeding completely; in 9 it ceased in the first twenty-four hours. Deaths in massive and continued hemorrhage from all causes may be considered as 15 per cent and deaths from exsanguinating hemorrhage in ulcer about 12 per cent. In this 12 per cent records suggest that in about 3 out of 12 cases pyloric obstruction or marked relaxed condition of the stomach from ulcer exists. To these 3 cases out of 12, about 2 more are due to carcinoma causing dynamic obstruction or delay of transit through the pyloric region. The continuation then of pyloric

obstruction seemingly becomes an important factor in the control of deaths from massive and continued hemorrhage.

TABLE I

CASE	LENGTH OF TIME AFTER FIRST VOMITING AND OPERATION (HOURS)	STOPPING OF HEMORRHAGE AFTER GASTRO-ENTEROSTOMY (HOURS)*	CAUSE		RECOVERY FROM CONTINUED HEMORRHAGE
			ULCER	CARCINOMA	
1	14	5	+		+
2	37	9	+		+
3	26	4½	+		+
4	41	5	+		+
5	60	60		+	+
6	43	7	+		+
7	71	5	+?		+
8	64	0		+	
9	52	50	+		+
10	49	54	+		+
11	38	5	+		+
12	29	6	+		+
13	34	12	+?	+	+
14	22	6	+		+
15	19	10	+		+

*This was judged by passing a tube into the stomach, which after operation was not done within an hour or two, frequently, or the tube was kept in continuously. Therefore, the figures are only approximate.

It must be evident that in the majority of these cases the diagnosis of pyloric obstruction would not be easy. As a rule the patient is in considerable mental distress, the friends agitated, or the patient so weak and dyspneic that detailed questioning is not satisfactory. When one can obtain information or when there has been an x-ray diagnosis of pyloric obstruction or the presence of an ulcer or palpable mass, it is suggestive of pyloric obstruction. As a rule such information is not on hand, and, because of the nature of the case, x-ray examination is not practicable. If in the past history one can suspect the presence of ulcer of long standing and if vomiting has been present, or if there had been attacks of tarry stools, suspicion may be aroused. As a rule, though, the case looks like the more common instance of gross gastric hemorrhage or melena as seen in gastric or duodenal ulcers without pyloric obstruction, cirrhosis of the liver, splenic conditions, etc., the type of case that usually is best handled by medical means. My experience has been that by the employment of a small gastric tube the best evidence of the continuation of hemorrhage is obtained. In the average case of frank gastric hemorrhage considerable clotted blood is found in the stomach and the hemorrhage tends to cease or manifests itself in diminishing ways. In pyloric obstruction, especially after emptying the stomach, the blood does not clot or the clots are very small and the bleeding continues steadily without much, if any, let-up until the end. Not too much dependence should be placed on this alone as far as suggesting pyloric

obstruction is concerned, because the fatal hemorrhage case without pyloric obstruction would continue in the same way. Thus, this observation in a diagnostic sense must be taken only as additional or suggestive information and not as total proof of pyloric obstruction. In my experience there are three methods of observing steadiness of bleeding: First, the tube is to be kept continually in the stomach and drainage instituted outside during the time of the bleeding, as has been suggested. Second, hemoglobin estimations should be made with or without erythrocyte counts every few hours, a procedure which is troublesome and not entirely to be depended upon because both may not show a progressive drop even though the hemorrhage continues. Third, allow vomiting spells to occur to suggest continued bleeding. In this the second vomiting and subsequent spells may not occur for a number of hours and the case may be carried on to the third or sixth day when the patient is a bad risk for surgery, even after blood transfusions. All that is necessary in the tube method is for a nurse to watch the steadiness of the bleeding. One can then tell during the first, second, or third day whether the bleeding is steady, usually in plenty of time for surgery, which, in the opinion of many surgeons, should be performed in every continued bleeding case irrespective of cause. The tube should be left in for a day or two, because, in some instances, the hemorrhage seemingly ceases for a few hours and then starts again. This bleeding, down to short-time stopping periods, probably is largely occasioned by blood depletion and is seen more frequently several days after the initial hemorrhage.

In the 11 ambulance cases noted, 8 were in the thin, undernourished type of individual so characteristic of gastroduodenal ulcer, especially when pyloric obstruction exists. Three were well nourished; 2 of these eventually were proved to have an extensive gastric carcinoma, the diagnosis being made at the time of the gastroenterostomy in 2, and several months afterwards in the third. Yet in each one of the entire group, visible peristalsis was present. As a rule this was not so marked as one commonly sees in pyloric obstruction, and it was necessary to watch very closely to observe it. The waves do not cross in a successive way from the left costal arch across the epigastrium to the pyloric region, the bulge advancing into a depression distal to it. Instead, there is a slight peristaltic roll, mostly perceptible at the costal margin and disappearing and not advancing perceptibly to the center of the abdomen. In 4 cases a slight bulging, rather indefinite, seemed to occur at the center and then disappeared. All of the cases had a distinct pyloric obstruction. It seemed probable that the presence of hemorrhage modifies the vigor and course of the waves. The observation of a bulging due to gastric dilatation was observed in 7 and was not present in 8 of the whole series. Obviously, as time went on, the general symptoms of continued hemorrhage were present.

CONCLUSIONS

Gross and continued hemorrhage from peptic ulcer or from any pathology in which pyloric obstruction is present is a condition of alarm which calls for surgery and not medical treatment. In this it is desirable that operation be performed early rather than late, preferably during the first seventy-two hours after the initial vomiting of blood. With whatever surgery is done, a gastroenterostomy seems necessary to permit the stomach walls to collapse and establish tonus, seemingly an essential for the control of hemorrhage in these cases. Watching the course of the bleeding by means of a tube in the stomach is the best and a safe method to diagnose continued bleeding. Visible peristalsis of a modified type seems to be present in all the cases. Allowing such cases, especially those in late middle age and older, to continue on medical handling has a higher rate of mortality than those operated upon promptly.

REFERENCES

1. Christiansen, Tage: On Massive Hemorrhage in Peptic Ulcer. Acta. med. Scandinav. **84**: 374, 1935.
2. De la Viesca, P.: Die grosse Magenblutung, Arch. of Verdauungskr. **58**: 22, 1935.
3. Meulengracht, E.: Treatment of Hematemesis and Melena With Food; the Mortality, Lancet **2**: 1220, 1935.
4. Hinton, J. W.: Massive Hemorrhage in Peptic Ulcer, Ann. Surg. **101**: 856, 1935.
5. Westermann, J. J.: Surgical Aspects of Bleeding Gastric and Duodenal Ulcer, Ann. Surg. **101**: 1377, 1935.
6. Goldman, L.: Gross Hemorrhage from Peptic Ulcer, J. A. M. A. **107**: 1537-1542, 1936.

PSOAS ABSCESS OF THE APPENDIX

HORACE MCCORKLE, M.D., SAN FRANCISCO, CALIF., AND
JEAN STEVENSON, M.D., CINCINNATI, OHIO

(From the Department of Surgery of the College of Medicine of the University of Cincinnati and the Cincinnati General Hospital)

THE common sites of both intra- and extraperitoneal abscesses that may originate from the perforated appendix are well known. Less frequently abscesses of appendiceal origin extending as far up as the thorax and as low as the thigh have been described. This case is an example of the latter type.

CASE REPORT.—CGH, 65601, a white male, aged sixty-seven years, entered the hospital on Dec. 11, 1936. He gave the history of a severe aching pain in the region of the right hip of about two weeks' duration. No abdominal pain, nausea, vomiting, or other symptoms of gastrointestinal disease could be obtained. A swelling with tenderness and a dusky redness had appeared over the region of the right upper thigh and hip about ten days before his entry into the hospital, and this confined him to his bed. Three days later he had a severe chill. Examination revealed a pale, thin old man. The abdomen was scaphoid and there was very slight tenderness in the right lower quadrant. No spasm or rebound tenderness was present. No abdominal masses could be palpated. The skin over the region of the right greater trochanter and extending over the anterior aspect of the upper thigh to the groin was red, tender, tympanitic, and greatly distended by a large fluctuant, gas-containing abscess beneath its surface. The largest diameter of this abscess was about eight inches. In one small spot the skin was necrotic and this permitted the seepage of a small amount of foul *B. coli* pus and bubbles of gas from the cavity of the abscess. The right inguinal glands were enlarged and quite tender. There was a soft pitting edema of the entire right lower extremity, but no edema was present on the left. Rectal examination was not remarkable. The heart and lungs were thought to be within normal limits for a man of his age. The peripheral vessels showed some evidence of arteriosclerosis. Blood pressure, 120/70. A few carious snags were all that remained of his teeth. His temperature varied from 98° to 100.6° F. White blood count, 12,250 per c.mm. A diagnosis of abscess of the thigh probably of appendiceal origin was made. On Dec. 12, 1936, he was taken to the operating room where the abscess was incised and evacuated of several ounces of thick foul *B. coli* pus and some gas. By palpation within the abscess cavity, it was found to extend toward the abdomen beneath Poupart's ligament, along the course of the iliopsoas tendon and lateral to the femoral vessels. Three cigarette drains were placed in this cavity beneath Poupart's ligament. His course was septic with temperature readings as high as 102° F. until Dec. 25, 1936, when he became afebrile and remained so. Blood culture taken Dec. 21, 1936, grew no organisms. The wound was treated at first with irrigations of physiologic salt solution and later with Dakin's solution. The edema of the leg subsided. The course of his illness was complicated by a senile psychosis that has improved but has not entirely cleared as yet. Barium enema performed on Jan. 14, 1937, revealed no evidence of organic disease. Roentgen ray examination of the spine revealed no destructive lesion. On

Received for publication, June 6, 1937.

Jan. 16, 1937, skin grafting of the granulating area was attempted but the patient destroyed the work. Since then the wound has closed slowly by granulation. On Feb. 11, 1937, a laparotomy was undertaken with general anesthesia through a small lower right rectus incision with the idea of removing the appendix in interval. The appendix was found in the retrocecal position and measured about three inches in length. The tip was surrounded by numerous adhesions which were bound to the posterior parietal peritoneum overlying the psoas muscle just lateral to the iliac vessels. In the course of separation of these adhesions a small abscess containing about

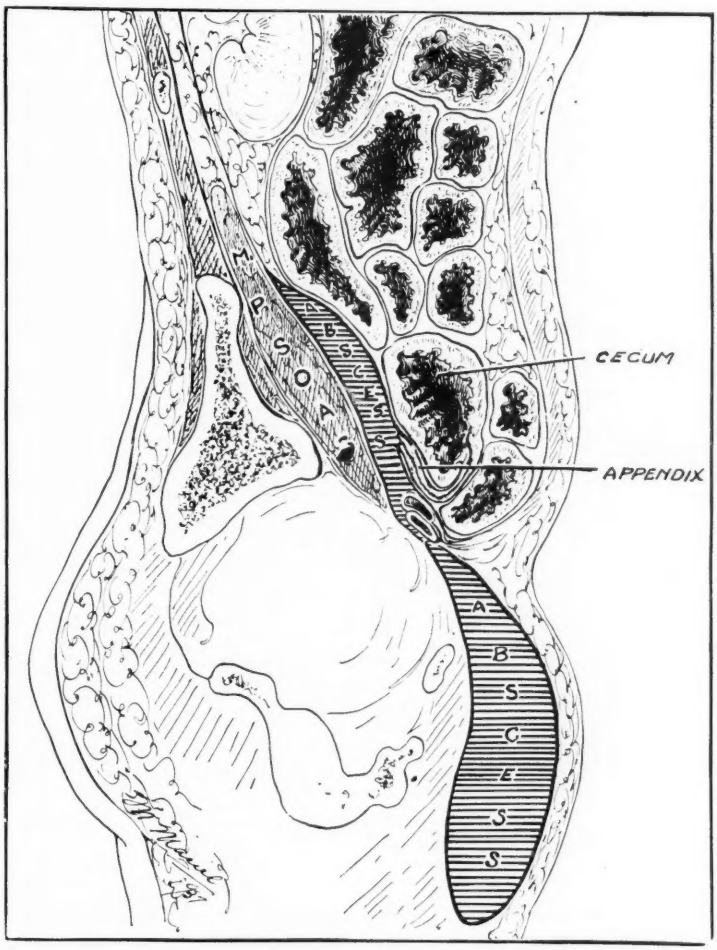


Fig. 1.—An illustrative sagittal section showing the retroperitoneal tip of the appendix and the resultant psoas abscess dissecting beneath Poupart's ligament to present in the thigh.

5 c.c. of thick white purulent material (culture later grew *B. coli*) was encountered. It was apparent that the appendix had ruptured at its tip into the psoas sheath. When the appendix had been dissected away, an irregular granular defect about 2 cm. in diameter was left on the surface of the psoas muscle. Appendectomy was performed. The abdominal wound was closed in layers with catgut without drainage. Postoperative convalescence was uneventful. Pathologic examination of the appendix revealed evidence of recent inflammation with healing by scar formation.

The presence of numerous foreign body giant cells suggested the possibility of tuberculosis, but a careful study of slides prepared by special staining methods failed to substantiate this.

In 1642 Saracenus[3] in a letter to a friend, a medical associate, told of the case of a fifty-year-old woman in whose right groin an abscess formed and ruptured spontaneously. The wound discharged at first foul pus and finally fecal material, half-digested food, and lumbricoid worms. The fistula finally healed and she recovered.

Fig. 2.—An illustration of the operative findings two months after draining the abscess of the thigh. A small chronic abscess filled with inspissated pus was found on the psoas muscle and surrounding the retroperitoneal tip of the appendix.

Copeland[3] in 1813 described a fecal abscess that developed in the right groin. It was opened with poultices and some weeks later an oval calculus was extracted from the fecal fistula which then healed.

In 1865 Buck[3] opened a "peri-typhlitic" abscess pointing in the right groin below Poupart's ligament. From this opening a pin was subsequently discharged.

Kelly[4] in his volume *The Vermiform Appendix and Its Diseases* published in 1905 describes psoas abscesses originating from appendicitis in his discussion of retroperitoneal abscess. He tells also of one remarkable case of G. W. Crile in which "the abscess extended from the

right iliac fossa down the inner aspect of the thigh to the popliteal space, where there was a large collection of pus."

John B. Deaver[3] in the 1914 edition of his *Appendicitis: Its Diagnosis and Treatment,* states regarding retroperitoneal appendiceal abscesses: "Such retroperitoneal abscesses sometimes give rise to the most extensive phlegmonous infiltration. Following the course of the iliac vessels they may present themselves beneath Poupart's ligaments; . . ."

Recent references to cases of abscess of this type are difficult to find. Leon Cohen-Solal,[2] 1936, in a paper on "Acute Primary Suppurations Developing in the Sheath of the Iliopsoas" remarks that "the infection is usually on the right side, possibly because appendicitis is frequently the original focus."

DISCUSSION

Deaver[3] gives four possible causes for the formation of retroperitoneal appendiceal abscesses:

1. Penetration or perforation of a completely retroperitoneal appendix.
2. Perforation into the mesoappendix or by extension of septic processes through the blood vessels or lymphatics of the mesoappendix.
3. "Such retroperitoneal suppuration may also occur in some cases in which rather firm adhesions bind the appendix to the posterior layer of the peritoneum. In these cases this posterior layer of the peritoneum may have become so altered by inflammation that in the event of perforation, it offers but little resistance to the advances of virulent bacteria and their toxins. Being less resistant than the firm adhesions, it gives way first, and there thus occurs a perforation of the appendix, directly through its peritoneal coat, some adhesions and the posterior layer of the peritoneum into the retroperitoneal connective tissues. A retroperitoneal abscess results, without any associated intraperitoneal suppuration."
4. "Retroperitoneal abscesses may occur secondarily by perforation through the posterior layer of the peritoneum of an abscess that originated intraperitoneally."

In the case reported in this paper, the finding of the tip of the appendix adherent to the psoas would seem to indicate that the acutely inflamed appendix had perforated into the psoas sheath in some way similar to the third mechanism described by Deaver. The presence of the small abscess might, however, indicate the fourth mechanism as most likely in this case. In either event the septic material would have passed down the psoas sheath, beside the iliac vessels, beneath Poupart's ligament to present, as it finally did, a large abscess of the thigh.

The difficulty of diagnosing such a case without a suitable history for appendicitis is obvious. The causes of retroperitoneal sepsis are many (*1* and *2* above) and the appearance of psoas abscesses from

sources other than the appendix is undoubtedly most common. The other possible sources of psoas suppurations should therefore be carefully ruled out by history, examination, laboratory, and roentgen ray studies before the appendix is to be suspected. The pus from the abscess must be of the foul type often seen in appendiceal abscess. Gas may be easily demonstrable in the abscess. When these conditions have been observed, the removal of the interval appendix may verify the diagnosis as it did in our case.

SUMMARY

A case report is given in which a psoas abscess presented on the right thigh and contained gas and foul *B. coli* pus like that so often found in appendiceal abscess. After ruling out other possible sources for the origin of the infection, laparotomy with appendectomy was performed. An interval appendix, the tip of which was adherent and perforated into the psoas sheath, was found, believed to be the cause of the disease, and removed. A brief discussion of some of the available writings about similar cases is given.

CONCLUSION

Abscess of the thigh may arise from the perforation of the appendix into the psoas sheath by gravitation of the septic material down its course beneath Poupart's ligament.

REFERENCES

1. Baer, Wm. S., Bennett, Geo. E., and Nachlas, I. Wm.: Non-Spinal Psoas Abscess, J. Bone & Joint Surg. **5**: 590-600, 1923.
2. Cohen-Solal, Leon: Acute Primary Suppurations Developing in the Sheath of the Iliopsoas, Rev. de chir., Paris **55**: 534, 1936; abstracted in Surg., Gynec. & Obst. **64**: 162, 1937.
3. Deaver, John B.: Appendicitis: Its Diagnosis and Treatment, Ed. IV, Philadelphia, 1914, P. Blakiston's Son & Co., pp. 12, 16, 35, 136, 137.
4. Kelly, Howard A.: The Vermiform Appendix and Its Diseases, Philadelphia, 1905, Wm. B. Saunders Company, pp. 314, 315, 205.

RIGHT RETROMESOCOLIC HERNIA

BÉLA HALPERT, M.D., NEW ORLEANS, LA.

(From the Department of Anatomy, Johns Hopkins University, and the Department of Pathology and Bacteriology, the School of Medicine, Louisiana State University)

THE condition here described is one of the rarest of intraperitoneal hernias; it was discovered during the routine anatomic study of the body of a thirty-five-year-old negro woman (C. A. 484 E) who, according to the record, died of "drunkenness." No other history was available. The disposition of the small intestine was identified as a malposition acquired during the rotation period of the development of the gut resulting in a right retromesocolic hernia.

The peritoneal cavity revealed the usual disposition of the upper abdominal organs. The stomach and the supramesocolic portion of the duodenum appeared dilated. The former measured 16 cm. along the lesser curvature and 56 cm. along the greater curvature which extended to the level of the iliac crests. The supramesocolic portion of the duodenum was 7 cm. long with a circumference of 7 cm. There was perfect fusion of the layers of the greater omentum which covered the lower abdominal organs. Reflection of the greater omentum and of the transverse colon with its mesocolon disclosed the relations shown in Fig. 1.

The cecum lay on the linea terminalis with the appendix in a craniomedial position. The ascending colon was of usual length and at the hepatic flexure formed an acute angle with the transverse colon. The latter was caudoconvex and continued at the splenic flexure into the descending colon. This, the sigmoid colon, and the rectum were in their usual positions. The right upper compartment of the peritoneal cavity below the root of the transverse mesocolon contained 90 cm. of the terminal ileum which at this point emerged from the opening of a peritoneal sac. The opening lay on the right side of the vertebral column directed anteriorly and medially, measured 7 by 5 cm., and had stoutly thickened margins. In addition to the terminal ileum a loop of jejunum passed through the opening of the sac. The left compartment of the peritoneal cavity below the root of the transverse mesocolon contained 134 cm. of jejunum. The cranial end of this segment of small intestine left the sac at the upper and anterior margin of the opening; the caudal end returned at the lower margin, while the terminal ileum emerged from behind. The sac was on the right side of the vertebral column and measured 20 by 16 cm. It formed a blind pouch of peritoneum containing the inframesocolic portion of the duodenum (22 cm. long) with the initial 15 cm. of the jejunum in its upper part and 110 cm. of col-

Received for publication, November 10, 1937.

lapsed loops of jejunum and ileum in its lower part (Figs. 2 and 3). There were no adhesions between the loops. At the point of passage through the opening of the sac, the circumference of the jejunum was reduced to 4 cm.—i.e., half the circumference of that situated outside the sac. Within the thickened craniolateral margin of the anterior wall of

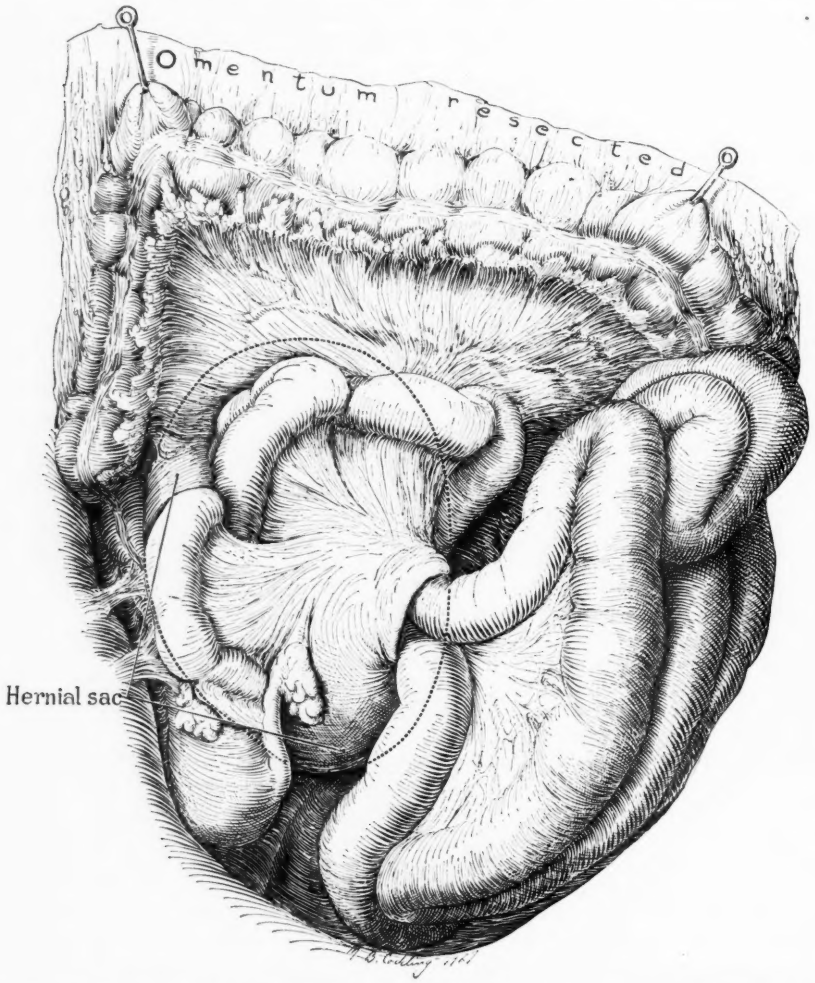


Fig. 1.—View of the lower abdominal organs after reflection of the greater omentum and of the transverse colon with its mesocolon. The right and upper compartment contains 90 cm. of the terminal ileum which emerges from the opening of the peritoneal sac together with a loop of jejunum, contained in the left compartment. The outlines of the sac are dotted.

the sac lay the ileocolic artery and vein. The opposite margin of the opening was made up of a firm double fold of mesentery.

Detailed dissection of the branches of the celiac axis, of the superior and of the inferior mesenteric arteries disclosed no unusual variations in their courses. The inferior mesenteric vein joined the superior mes-

enteric vein which united with the splenic to form the portal vein. Along the left side of the aorta an accessory vein connected the left common iliac with the left renal vein (remnant of the left caudal cardinal vein).

COMMENT

There are seventeen cases of right duodenal hernia enumerated in the second edition of Moynihan's monograph, *On Retro-Peritoneal Hernia,* published in 1906.[1] The first of these is credited to Klob whose report appeared in 1861. According to Nagel, twenty-nine authentic cases of right paraduodenal hernia were published up to 1923.[2] In the same year Andrews listed sixty cases that had been reported since 1906, but he made no attempt to classify them into right or left "as this has in many cases seemed a matter of great doubt." Andrews concluded that duodenal hernia is a congenital anomaly due to imprisonment of the small intestine beneath the mesentery of the developing colon.[3] In 1925 Brown listed thirty-two authentic cases of right duodenal hernia.[4] Haymond and Dragstedt described a case in 1931. This case, "which formerly would probably have been considered an intra-abdominal hernia is now more logically explained on the basis of malrotation of the midgut loop in the second stage of rotation."[5] Their case is not included in Exner's list of forty cases reported up to 1932.[6] Authentic cases have been presented since by Harris,[7] Halliwell,[8] Takashima, Hirano, and Ikeda,[9] Bryan,[10] Schildt,[11] Foote,[12] and Averbach.[13] These, together with the present one, bring the number of authentic cases to forty-nine.

The type of malposition of the small intestine presented here is apparently a developmental anomaly, due to a faulty orientation of the developing gut during that period of its rotation when the cecum migrates towards the right iliac fossa and the hepatic flexure becomes fixed. The failure of the caudal and medial two-thirds of the ascending mesocolon to fuse with the parietal peritoneum leaves a pocket enclosing the loops of the small intestine. The opening of this pocket, which is the hernial sac, points towards the left and the pelvis. Its anterior wall is the ascending mesocolon, hence the name *hernia retromesocolica dextra.* The anterior wall of the hernial sac being the ascending mesocolon, it naturally contains the vessels tributary to the ileocecal region and to the right half of the colon; namely, the ileocolic and the right colic arteries and veins. The posterior wall is formed by the parietal peritoneum. The hernial sac has nothing to do with the duodenum since the latter attains its usual shape, position, and peritoneal relationship.

Perhaps in this case, as in almost all of the other illustrated cases, the hernial sac at first contained all of the small intestine with the exception of a segment of the terminal ileum. In this instance, however, a loop of jejunum escaped later through the mouth of the hernial sac and remained located in the peritoneal cavity outside of the sac. This sequence

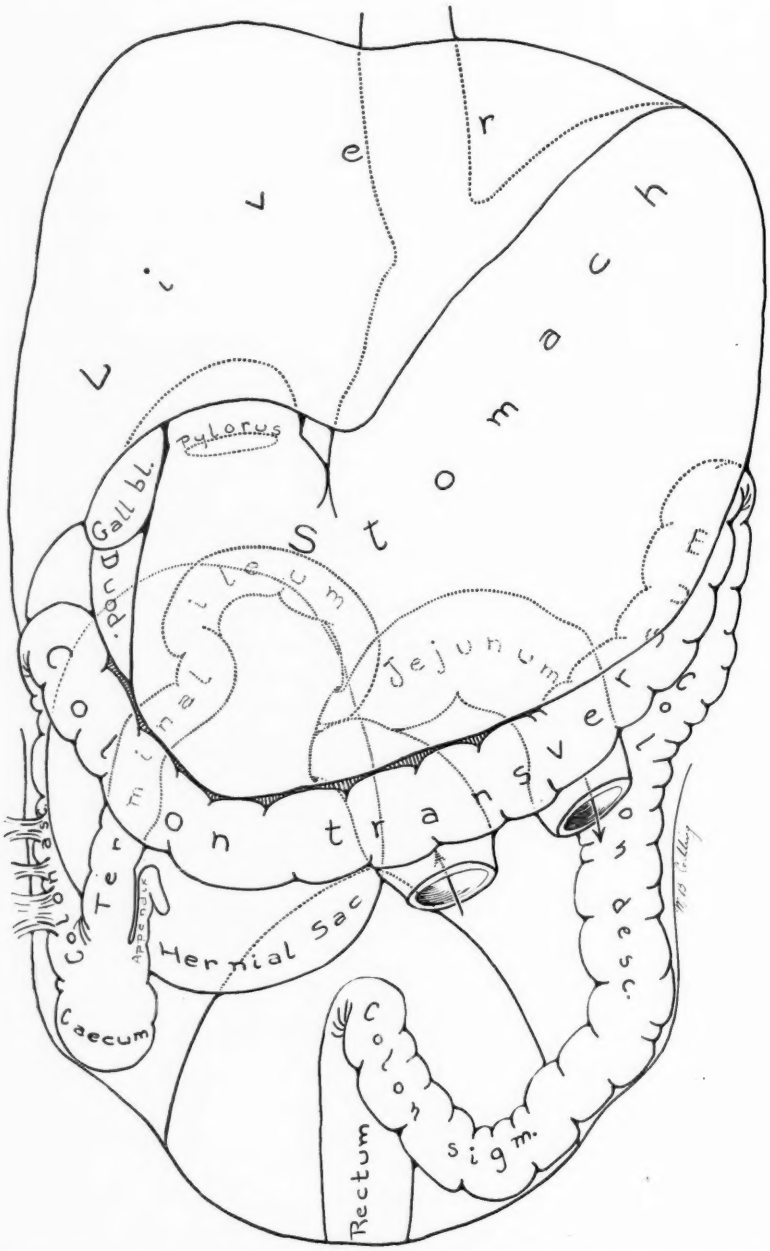


Fig. 2.—The cranial end of the jejunum leaves the sac at the upper and anterior margin of the opening; the caudal end returns at the lower margin, while the terminal ileum emerges from behind.

Fig. 3.—The location of the loops of the small intestine within and outside the sac is indicated.

of events seems more reasonable than the alternate one; namely, that all of the small intestine herniated into the peritoneal sac leaving only a segment of the jejunum outside. As far as can be ascertained, this is perhaps the only reported case in which the above situation pertained; namely, that a loop of small intestine escaped from the hernial sac into the peritoneal cavity through the mouth of the sac.

SUMMARY

Malposition of the small intestine in a peritoneal sac behind the ascending mesocolon is described and interpreted as a right retromesocolic hernia.

REFERENCES

1. Moynihan, B. G. A.: On Retro-Peritoneal Hernia, New York, 1906, William Wood & Company.
2. Nagel, Gunther W.: Right Paraduodenal Hernia, J. A. M. A. **81**: 907, 1923.
3. Andrews, Edmund: Duodenal Hernia—A Misnomer, Surg., Gynec. & Obst. **37**: 740, 1923.
4. Brown, Francis R.: Right Duodenal Hernia: With Report of a Case Successfully Operated on, the Fourth Recorded Recovery, Brit. J. Surg. **13**: 367, 1925.
5. Haymond, H. E., and Dragstedt, Lester R.: Anomalies of Intestinal Rotation: A Review of the Literature With Report of Two Cases, Surg., Gynec. & Obst. **53**: 316, 1931.
6. Exner, Frederick B.: The Roentgen Diagnosis of Right Paraduodenal Hernia, Am. J. Roentgenol. **29**: 585, 1933.
7. Harris, V. C. J.: Retro-Peritoneal Hernia, Lancet **2**: 240, 1932.
8. Halliwell, A. C.: Right Paraduodenal Hernia, Brit. J. Surg. **21**: 398, 1934.
9. Takashima, R., Hirano, H., and Ikeda, M.: Über einen Fall von Hernia paraduodenalis dextra mit W-förmiger, Inkarzeration des Dünndarmes, Zentralbl. f. Chir. **62**: 922, 1935.
10. Bryan, Robert C.: Right Paraduodenal Hernia, Am. J. Surg. **28**: 703, 1935.
11. Schildt, Evert: Über eine ungewöhnliche Form von Hernia retroperitonealis (Hernia mesenterico-parietalis dextra—Broesike), Acta chir. Scandinav. **76**: 35, 1935.
12. Foote, Frederick S.: Mesenterico-Parietal Hernia, California & West. Med. **43**: 292, 1935.
13. Averbach, Bertram F.: Right Paraduodenal Hernia, Am. J. Surg. **35**: 128, 1937.

REPAIR OF DIRECT INGUINAL HERNIA BY OSTEOPERIOSTEAL GRAFT TO THE PECTINEAL LINE OF THE PUBIS

J. Ross Veal, M.D., and Dan D. Baker, M.D., New Orleans, La.

(From the Departments of Surgery and Anatomy of the School of Medicine, Louisiana State University, and Charity Hospital of Louisiana in New Orleans)

THE results of the surgical repair of direct inguinal hernia by the operations thus far devised have proved disappointing. Andrews and Bissell,[1] from a follow-up of their cases and a review of the literature, reported that there was a recurrence rate of 20 per cent. Such a high percentage of failures suggests an anatomic rather than a technical deficiency in the procedures commonly used.

The various procedures now in use for the repair of direct inguinal hernias all have similar anatomic principles.[2] Wolfler, in 1892, advocated incising the anterior rectus sheath and drawing the muscle down to the inguinal ligament and suturing it there. In 1898 Bloodgood described an operation in which a portion of the rectus muscle and its sheath were drawn down and sutured, with the conjoined tendon and internal oblique, to the inguinal ligament. Halsted, Hotchkiss, Lusk, and Berger secured a triangular flap from the anterior sheath of the rectus, turned it down, and sutured it to the inguinal ligament. Blake, in 1900, exposed the lower rectus muscle and sutured it to the inguinal ligament. He next brought down the internal oblique muscle behind the cord, sutured it to the inguinal ligament, and then overlapped the edges of the aponeurosis. Downes, in 1911, utilized a similar procedure suturing the rectus and internal oblique muscles to the inguinal ligament. All of these operations attempt to form a buttress by attaching either the conjoined tendon, internal oblique muscle, rectus muscle or sheath, or a combination of these structures to the inguinal ligament. The use of fascia as sutures in the place of silk or catgut has many advocates, but even with this substitution the percentage of failures has not been materially reduced.

A review of the anatomy of the structures involved in a direct inguinal hernia will show that, after such methods of repair as have been mentioned, there still remains a defect over the pectineal line of the pubis. The normal support afforded by the conjoined tendon over that region is lost. A direct inguinal hernia protrudes through Hesselbach's triangle, medial to the deep inferior epigastric artery. The principal structures involved are the conjoined tendon and transversalis fascia.

Received for publication, January 10, 1938.

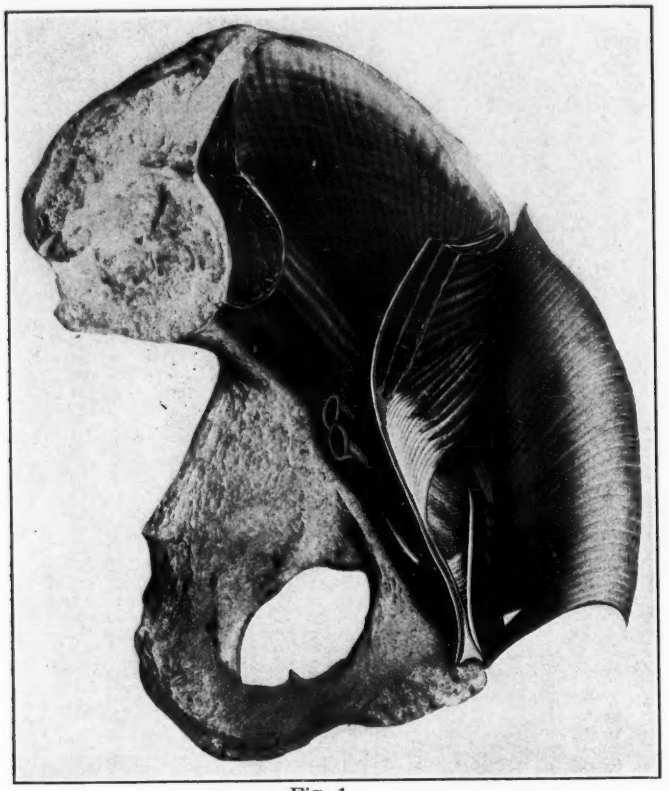


Fig. 1.

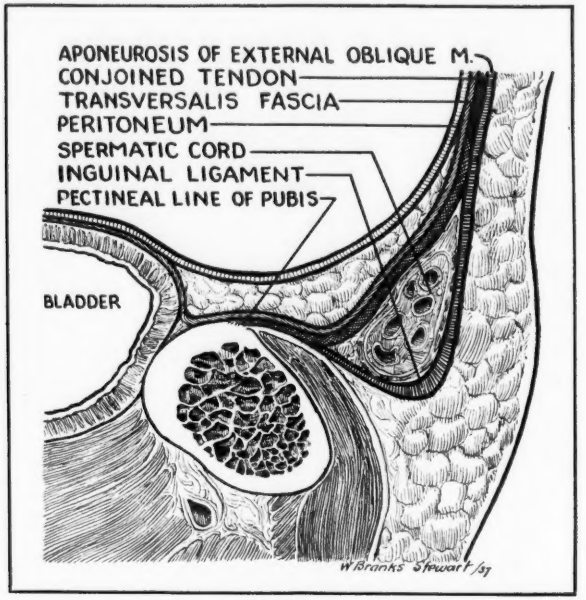


Fig. 2.

Fig. 1.—Drawing of inguinal region showing the formation of the conjoined tendon and its attachment to the pubis. Note the extension of the attachment along the pectineal line giving the anterior abdominal wall strong support posterior to the external inguinal ring.

Fig. 2.—Diagram of a sagittal section through the pelvis 1½ inches to the right of the middle anterior abdominal line, showing the blending of the transversalis fascia to the posterior surface of the conjoined tendon and their attachment to the pectineal line of the pubis.

The conjoined tendon is formed by the union of the aponeurosis of the obliquus internus abdominis and transversus abdominis muscles. It is attached to the crest, the spine, and a portion of the pectineal line of the pubis. It is also loosely attached to the shelving edge of the inguinal ligament. The union to the pectineal line is very firm. The conjoined

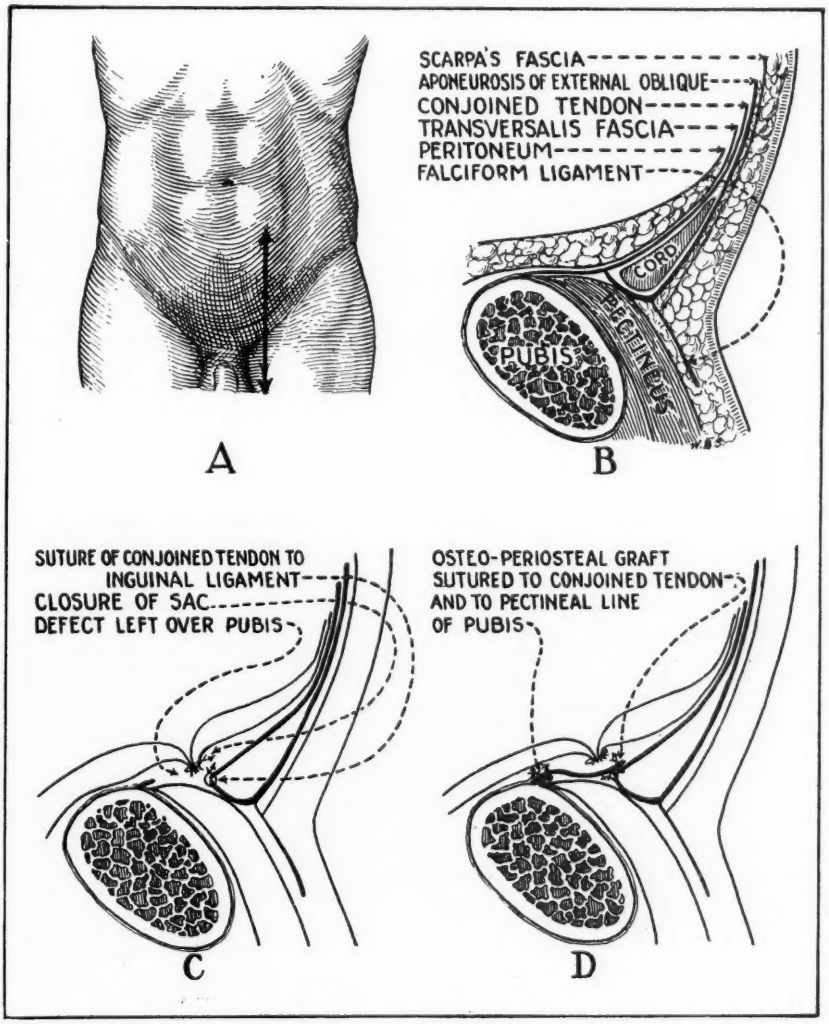


Fig. 3.—*A*, arrows indicate position of sagittal sections *B*, *C*, and *D* 1½ inches lateral to the middle anterior abdominal line; *B*, the normal relations of shelving portion of the inguinal ligament to the conjoined tendon and the pectineal line of pubis; *C*, illustration of the defect over the pectineal line after the usual operation for repair of a direct hernia; *D*, showing the closure of defect by means of an osteoperiosteal graft.

tendon forms a strong support to the anterior abdominal wall behind the external inguinal ring (Fig. 1). The transversalis fascia is attached inferiorly to the outer two-thirds of the shelving edge of the inguinal ligament and to the crest and the medial half of the pectineal line of the

pubis, posterior to the conjoined tendon. The fascia is very thin medial to the femoral vessels and is adherent to the posterior surface of the conjoined tendon. (Fig. 2.) Keith, as cited by Rives,[3] has demonstrated on cadavers of newborn infants that, when an inguinal hernia exists at birth, the conjoined tendon is not attached to the pubis but is attached higher up on the border of the rectus sheath.

For a hernia to occur through Hesselbach's triangle, there must be either an anatomic variation in the insertion of the conjoined tendon or there must develop some weakness of the transversalis fascia and conjoined tendon in this region. The hernia pushes the transversalis fascia forward and the conjoined tendon is displaced forward and medially. These structures become thin as the hernia enlarges. It may break through the transversalis fascia and displace or disrupt the attachment of the conjoined tendon to the pectineal line of the pubis. Such a hernia

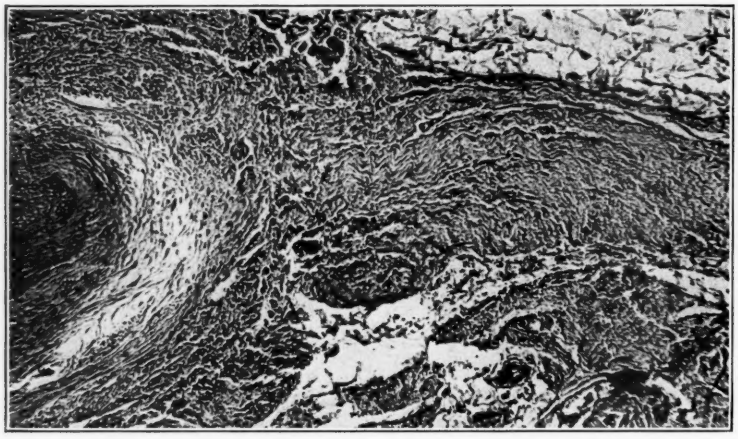


Fig. 4.—Low-powered photomicrograph showing the union of osteoperiosteal graft to the tip of a transverse process in the dog.

when examined will be found to glide over the superior surface of the pubis and the strong sheet of the conjoined tendon normally present will be missing.

The loss of the support of the conjoined tendon and of the transversalis fascia over the pectineal line of the pubis is then the pathologic basis for the development of a direct inguinal hernia. Any repair which does not reestablish this support along the pectineal line will leave an anatomic defect which may lead to recurrence of the hernia (Fig. 3*C*). In order to close this defect the repair should begin by building up a buttress from the pectineal line (Fig. 3*D*). It is very difficult and often impossible to fix any of the surrounding structures, such as the rectus sheath or conjoined tendon, to the pectineal line of the pubis. Therefore, it becomes necessary to use some type of free fascial transplant to overcome this defect.

From the works of MacEwen[4] and Gallie and Robertson,[5] it would seem that an osteoperiosteal strip grafted to bone or periosteum should become firmly united to that structure by dense fibrous tissue. This type of graft also forms a firm union with fascia and muscle by the formation of a fibrous tissue scar. These authors have also shown that

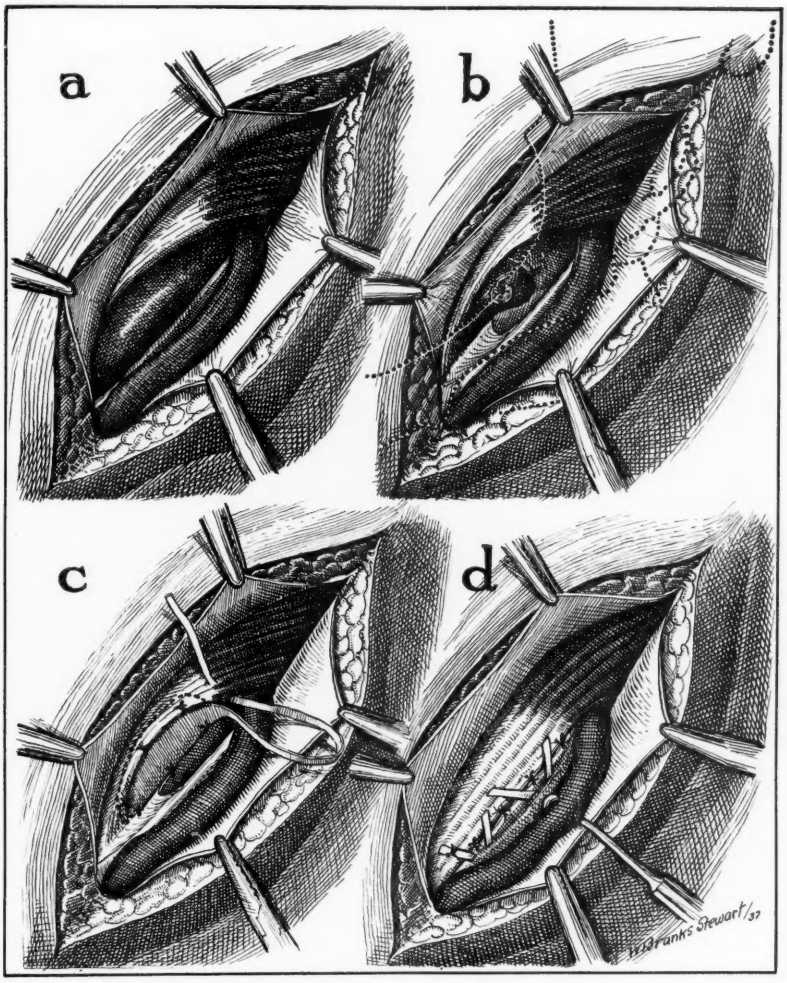


Fig. 5.—Drawings showing the steps in the repair of a direct hernia using an osteoperiosteal graft. *a*, exposure of the sac and retraction of the cord laterally; *b*, ligation of the sac; *c*, insertion of osteoperiosteal graft along the pectineal line of the pubis and showing the points of suture to conjoined tendon; *d*, use of the periosteal strip as a fascial suture uniting the conjoined tendon to the shelving portion of the inguinal ligament, behind the cord.

if periosteum, bone and periosteum, or bone alone is transplanted to structures where bone is not normally found, or where there is no function for it to perform, the bone will become absorbed and the graft will leave fibrous tissue scar. In a series of experiments on dogs we have found that the osseous portions of osteoperiosteal grafts transplanted

into muscle or attached to transverse processes of the spinal vertebrae have been gradually absorbed. However, there has been left behind a dense layer of fibrous tissue which has become firmly united to the surrounding structures. (Fig. 4.) Therefore, it would seem that osteoperiosteal grafts would serve admirably to repair the defect over the pectineal line of the pubis.

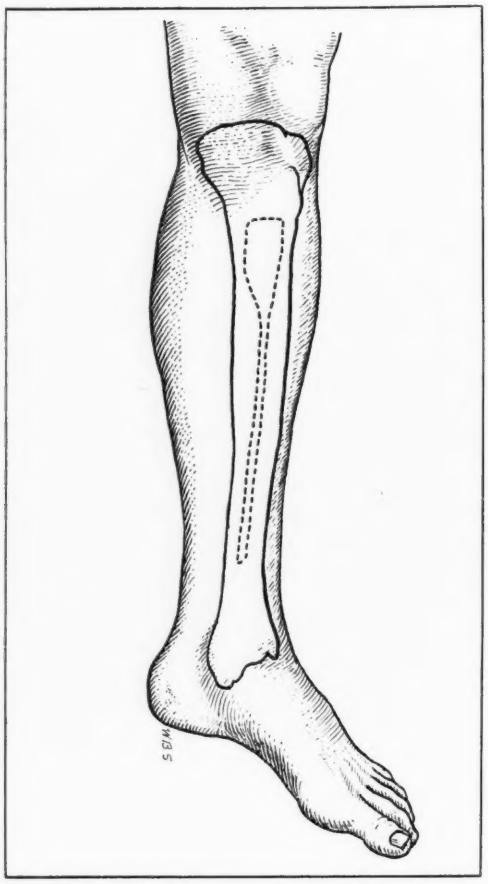


Fig. 6.—Drawing showing the origin of the osteoperiosteal graft from the anterior surface of the tibia. Note the shape of the upper end of the graft which is used to fill in the defect over the pectineal line of the pubis. The long tail portion is used as a fascial suture.

These principles have been used in the repair of a series of direct inguinal hernias in the following manner (Fig. 5): The usual oblique incision is made. The external oblique aponeurosis is divided and the hernia exposed. The cord is retracted laterally. The inferior epigastric artery is identified and in cases of large hernias is divided between ligatures just above the inguinal ligament. The sac is ligated with a purse-string suture and excised. Now the superior surface of the pubis is exposed by pushing the transversalis fascia and peritoneum backward.

The periosteal covering over the pectineal line of the pubis is divided with scalpel from the pubic spine to the margin of the femoral vessels. This incision extends through the periosteum, exposing the pectineal line of the pubis. Attention is now turned toward the preparation of a periosteal graft.

An incision is made over the medial border of the tibia, 8 to 12 inches in length. The anterior surface of the tibia is exposed. A full thickness osteoperiosteal graft is now removed (Fig. 6). The upper portion of the graft is made the size and shape to fit into the defect over the pectineal line of the pubis. This portion of the graft is made of the full thickness of the periosteum and also contains thin slips of bone. The long tail

Fig. 7.—X-ray of the pelvis made two weeks after repair of a direct hernia with osteoperiosteal graft. Arrows show the position of the osteoperiosteal graft along the pectineal line of the pubis.

part is made up only of periosteum. The graft is sutured first to the divided periosteum of the pubis with two to four sutures of chromic 0 catgut. It is then sutured to the posterior surface of the conjoined tendon. (Figs. 3*D* and 5*c*.) The long periosteal tail is used as a suture to draw the conjoined tendon down to the inguinal ligament. Two to four additional chromic No. 1 sutures are used to unite the conjoined tendon to the inguinal ligament. The cord is now replaced and the external oblique aponeurosis and skin closed. The skin incision in the leg is then closed, no attempt being made to close the periosteum.

This operation has been done on 14 patients. The first operation was done February 19, 1937. All wounds healed by primary union. X-rays made two weeks after the operation in each instance have shown

the graft at the site sutured to the pectineal line of the pubis (Fig. 7). Three months later, however, all the bone in the graft had apparently been absorbed. X-ray pictures made at this time failed to show any evidence of bone at the site of the graft. Physical examination revealed a very dense wall of fibrous tissue scar over the superior surface of the pubis. X-rays of the tibiae have shown no bone changes or any evidence of proliferation of the periosteum. Follow-up examinations on these patients have revealed no recurrences thus far. It is entirely too early to draw final conclusions. This preliminary report is made with the hope that others will try this procedure and thereby aid in determining its merits.

REFERENCES

1. Andrews, E., and Bissell, A. D.: Direct Hernia: A Record of Surgical Failures, Surg., Gynec. & Obst. **58**: 753-761, 1934.
2. Watson, L.: Hernia, St. Louis, 1924, C. V. Mosby Co.
3. Rives, J. D.: Inguinal Hernia: The Principles Upon Which Its Treatment Is Based, Internat. S. Digest **15**: 3-13, 1933.
4. MacEwen, W.: The Growth of Bone, Glasgow, 1912, James Maclehose and Sons.
5. Gallie, W. E., and Robertson, D. E.: The Repair of Bone, Brit. J. Surg. **7**: 211-261, 1919-1920.

AN EXPERIMENTAL STUDY OF THE EFFECTS OF X-RADIATION UPON ACUTE PYOGENIC INFECTION OF THE SKIN AND SUBCUTANEOUS TISSUES*

JOSÉ A. SOTO, M.D.,† ALEXANDER BRUNSCHWIG, M.D., AND F. W. SCHLUTZ, M.D., CHICAGO, ILL.

(From the Departments of Pediatrics and Surgery and the Division of Roentgenology of the Department of Medicine, The University of Chicago)

INTRODUCTION

THE beneficial effects of x-radiation upon a large variety of acute and chronic infections in man have been repeatedly cited in the literature for many years (bibliography by A. U. Desjardins). On the other hand, controlled experimental evidence for the efficacy of such treatment in acute pyogenic infections has been reported in but a relatively few instances.

Shaefer in a series of 22 rabbits observed the effects of 450 r of x-radiation in subcutaneous and intramuscular infection produced by injection of staphylococci. In 11 cases the irradiated lesions healed more rapidly than in control animals. In 7 cases the severity of the inflammation was reduced but healing was not accelerated. In 4 cases no differences were noted. Somewhat similar results were reported by Proto using 10 animals and 4 controls. Motojima, in the course of a study of the effects of x-radiation upon "chemical inflammation," also injected a series of 15 rabbits with staphylococci in two locations in each animal and exposed one of the foci to small doses of x-rays. In all but two instances the doses were substantially less than "1 erythema" and no differences were noted. In the two cases where one erythema dose was delivered, the severity of the process was reduced. Lacassagne and Vinzent infected rabbits with *Streptobacillus caviae* and observed that x-radiation led to eventual healing of the process which in control animals was ultimately fatal in all instances.

Except for the observations of Motojima, in the previous experimental work, controls consisted of animals injected with the bacteria and not irradiated. Apparently little attention was paid to the fact that quite appreciable variations obtain in the severity of infections induced in any series of animals injected with like amounts of the same organisms. It would appear that untreated lesions in the same animal having an irradiated lesion afford the best experimental control.

*This work was supported by a special grant from the Douglas Smith Foundation of the University of Chicago.

†Douglas Smith Fellow, University of Chicago.

Received for publication, December 28, 1937.

The authors' clinical experience in roentgenotherapy of acute and chronic pyogenic infections comprises, for the most part, furunculosis, carbuncle, cellulitis, and lymphadenitis. While in some instances a definite impression was obtained that the treatment was beneficial, final conclusions were impossible because of the great variation in the course of such infections observed clinically where roentgen therapy was not employed. For this reason a series of experiments were performed to test again the value of such treatment under controlled conditions.

EXPERIMENTAL

In the following experiments the irradiation was delivered at 200 kv., 25 Ma., 50 cm. F.S.D., and 1 mm. Cu + 1 mm. Al. Measurements expressed in r units in air.

The bacterial suspensions injected consisted of twenty-four-hour blood agar slants taken up in distilled water. It was felt that the use of distilled water would favor rapid diffusion of the bacteria in the foci of inoculation.

EXPERIMENT I.—Control experiments, 8 rabbits.

In 5 rabbits injections of 1/16 c.c. of a suspension of *B. coli* were made on the right posterior back over the left hip and on the left anterior back just back of the left shoulder. In 3 animals 0.5 c.c. of such a suspension was injected in a similar manner. In 3 cases only one point of injection was made in each area; in the others two adjacent injections were made, thus affording two foci of two injections each in the same animal. In twenty-four hours the injected sites exhibited irregular or oval elevations and erythematous areas measuring 0.6 to 1.5 cm. in diameter. The point of injection in the center of these areas appeared as a small yellowish spot. Subsequently the yellowish spot increased in size and the edematous areas decreased slightly, and by the fifth or sixth day a frank abscess not surrounded by edema was present. Small crusts then appeared over the central portions of the abscesses and the latter gradually resorbed during the subsequent twelve to thirty days (healing under crust). In some cases there was spontaneous rupture with discharge of purulent material.

There was some variation in the course of the inflammatory lesions in each animal. One of two adjacent foci often appeared smaller than its neighbor, but again on other days the differences would not be as appreciable in the same animal. In no instance did one pair of foci pursue a markedly different course than the other pair. Healing of all lesions in a given animal occurred at about the same time after injection. Considerable variation in the course and healing time occurred among the different animals.

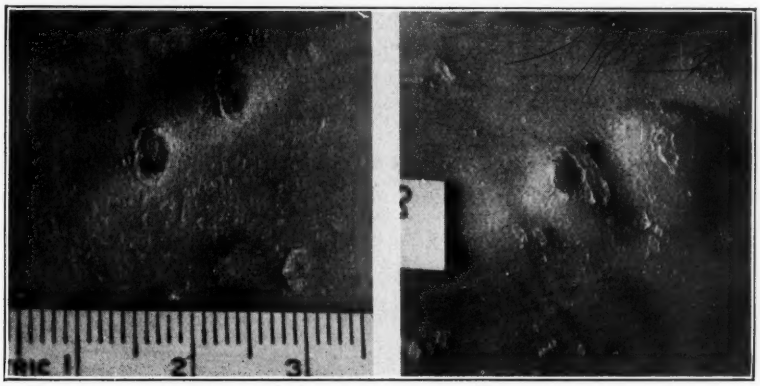
EXPERIMENT II.—Irradiation at various intervals in relation to intracutaneous injection of *B. coli* suspension in distilled water.

A. Irradiation twenty-four hours before injection: Six hundred r were delivered to an 8 by 8 cm. portal over the caudal portion of the right back in 7 rabbits. Twenty-four hours later 1/16 c.c. of the *B. coli* suspension was injected intracutaneously in two adjacent points in the irradiated area and two adjacent points cephalad on the left back, the latter to serve as controls for the former.

The subsequent course of the inflammatory lesions varied among the animals. In one instance the inflammation was always less intense in the irradiated field than in the control and healing was more rapid in the former. In 3 cases no dif-

ference was apparent between test and control lesions and in the remaining 3 the abscesses of the irradiated lesions appeared slightly larger than the controls, although final healing occurred at about the same time. The differences in size in the latter group, however, were within the limits of variation observed in the controls of Experiment I.

B. Irradiation within five hours after injection of the bacteria, 15 rabbits: In two areas on the back, one above the right hip and one above the left shoulder, two adjacent intracutaneous injections of 1/16 c.c. or 1/8 c.c. of distilled water-*B. coli* suspension were made, the same dose being used in a given animal. The posterior area was irradiated. In 12 instances the lesions in the posterior or irradiated field exhibited less edema and the abscesses subsequently developed were smaller than in the control areas in the same animal. In 1 case the differences were apparent twenty-four hours after irradiation; in the remaining 11 instances the differences were not appreciable until the third to fifth day. In most cases the irradiated lesions subsequently resorbed more rapidly than the controls and were healed a few days before the latter. In some instances final healing in the two areas occurred about the same time, even though the irradiated lesions were smaller.



A. *B.*

Fig. 1.—Illustrating one rabbit in Experiment II *B* (see text). Two foci of pyogenic inflammation were produced by intracutaneous injection of 1/16 c.c. suspension of *B. coli* in distilled water at two adjacent points on the animal's back—one focus posteriorly on the left side and one anteriorly on the right. Three hours after injection, the posterior group received 600 r x-radiation. Above photo taken five days later shows severity of inflammation in *A*, the irradiated lesions, to be quite appreciably less than in *B*, the nonirradiated controls in the same animal.

In 2 animals the irradiated lesions exhibited slightly more intense inflammation than the controls. In 1 of these an appreciable difference did not appear until about the tenth day and eventual healing occurred earlier in the control area. In the other the control area exhibited healing by the twelfth day, while the lesions in the irradiated area were not resorbed until the sixteenth day.

In 1 animal there was no difference between the irradiated and control lesions.

C. Irradiation of posterior area twenty-four hours after injection of bacteria as above, 10 rabbits: Consistent results were not obtained in this series, as in 3 instances healing appeared slightly delayed in the irradiated areas; in 2 instances healing of the irradiated areas appeared slightly accelerated, and in 5 instances no differences were observed.

D. Irradiation of the posterior area seven days after injection: Two small abscesses of approximate equal size (1.5 cm. in diameter) were present in each area as a result of 1/16 c.c. *B. coli* suspension injected intracutaneously, 6 rabbits. No differences were appreciable in the subsequent course of the lesions between the irradiated and control areas.

EXPERIMENT III.—Irradiation of foci of acute inflammation due to bacteria of relatively low virulence for the test animal.

Control observations using a strain of *Staphylococcus aureus* revealed this organism to provoke a much milder reaction and smaller suppurative foci than in the case of the strain of *B. coli* used above.

Irradiation was given immediately after injections, made as above to the posterior area in each of 6 animals. In 2 instances the irradiated foci exhibited less inflammation than the controls for two or three days following irradiation, but later no difference was appreciable between the test and control areas, and when healing occurred the size of the lesions was about the same. In 4 cases no difference was observed, healing taking place by the tenth to fourteenth day.

Fig. 2.—Injection of 0.1 c.c. croton oil intracutaneously on back of rabbit at two widely separated foci. Seven days later 600 r x-radiation to posterior focus, *R.* Photograph taken thirteen days after irradiation. Intense edema persists in control area, *C.*; only slight edema in irradiated area, *R.*

EXPERIMENT IV.—Irradiation of inflammatory foci where large numbers of virulent bacteria were injected.

This experiment was performed by Dr. B. H. Blocksom. Eight rabbits each received four intracutaneous injections, two on each side of the back, of 0.5 c.c. sterile water suspension of a virulent hemolytic *Staphylococcus aureus* prepared as described above. Markedly edematous indurated areas 2 to 2.5 cm. in diameter developed in twenty-four hours in the center of which necrosis and sloughing of the skin then occurred. One area on each side of the back was given from 300 to 600 r of x-radia-

tion, the same doses used in each animal. In some instances this was given one hour after injection and in others twenty-four to forty-eight hours later. In no instance were there appreciable differences between the evolution of the test and control lesions.

Microscopic study of sections from irradiated and control inflamed foci was made both where there were gross differences and where the two areas were the same at varying intervals following irradiation. No evidence was found in these sections that the irradiation had induced a widespread disintegration of leucocytes, especially lymphocytes. Where the irradiated foci were smaller, due presumably to irradiation, the process was not qualitatively different from the control areas. Smears from pus expressed from irradiated and control lesions likewise revealed no qualitative differences in the exudate.

Thus, because no evidence was obtained to indicate an irradiation effect upon the leucocytic exudate, the question of effects upon capillary permeability was next considered.

In a previous study of another nature in which croton oil was injected into rabbits' tissues, it was observed that this substance induced a very marked and widespread gelatinous-like edema in the subcutaneous tissues as well as an acute diffuse leucocytic infiltration, and finally skin necrosis and intense suppuration.

EXPERIMENT V.—Croton oil control experiments.

One-tenth cubic centimeter of croton oil was injected in two foci subcutaneously in 7 animals. One injection was made forward in the right back and the other was made caudad on the left side. The evolution of the inflammatory process was about the same in each area in the same animal. After five to seven days, marked edema over an area several centimeters in diameter was present and over the central portion of this a circular patch of beginning dry gangrene of the skin appeared. A few days later suppurating sinuses appeared at the margins of the crust. The latter then slowly separated leaving an ulcer which required three to four weeks to heal.

EXPERIMENT VI.—The effects of irradiation at various intervals upon the inflammation induced by subcutaneous injection of $\frac{1}{10}$ c.c. croton oil.

A. In 7 animals 400 r of x-radiation were delivered to the posterior right back. Twenty-four hours later two injections of croton oil were made, one anteriorly in nonirradiated tissue and one posteriorly in the irradiated field. Subsequent observations showed less intense edema in the irradiated areas in 3 animals; in 4 animals no distinct difference was noted. In all instances complete healing occurred about the same time, i.e., one month.

B. In 5 animals injected as above, 600 r of x-radiation were delivered to the posterior port immediately after the injection. By the sixth day the intensity of edema about the central necrotic skin patch was considerably greater in each case in the control than in the irradiated area. Subsequently this difference became less marked in 2 instances but persisted in the remaining 3 until healing occurred of all lesions at the same time approximately one month after injection.

C. Six hundred r were delivered to the posterior area twenty-four to forty-eight hours after subcutaneous injection of croton oil in 9 animals. In 7 instances the severity of the local edema was subsequently quite appreciably less in the irradiated than in the control areas; in 2 instances there was no difference. Final healing of the irradiated areas was not more rapid than the controls even where the reactions were less severe throughout the course of the lesions.

D. Four hundred r were delivered to the posterior area in 7 animals seven days after $\frac{1}{10}$ c.c. of croton oil was injected subcutaneously in two regions as above. At this time the edema was marked and equal in extent in each area. In 4 instances the

edema was considerably reduced by forty-eight to seventy-two hours after irradiation and subsequently resorption of the process was more rapid in the irradiated areas. In 3 cases no appreciable difference was observed between the test and control areas.

Thus the effects of irradiation upon croton oil inflammation are manifested by a reduction in the extent of the gelatinous like edema. This would indicate an effect of the irradiation upon capillary permeability in the region. Microscopic sections show no differences in the quality of the leucocytic infiltration, between those irradiated lesions where the edema had been reduced and the control areas where the edema was relatively much more intense.

Since the tissue reactions from croton oil injections were quite violent, further observations were made upon permeability effects in the capillaries where only a mild and brief disturbance in permeability was induced.

EXPERIMENT VII.—The effects of x-radiation upon histamine wheals.

One-tenth c.c. of histamine dihydrochloride was injected intracutaneously in two adjacent points in two separate areas on the backs of rabbits. One area was given 600 r of x-radiation; the other area served as a control. Preliminary tests revealed that where nothing was done to the skin all of the wheals disappeared about the same time in a given animal. Observations were made using in all 9 animals in which the disappearance of the histamine wheals in areas two to three hours, twenty-four, forty-eight, and seventy-two hours and seven days after irradiation was compared with control areas in the same animal. No appreciable differences were observed.

Additional experiments were conducted in which 600 r x-radiation was delivered to one ear of a rabbit, the other serving as control, and 1 per cent aqueous solution of trypan blue and pontamin blue injected into the marginal vein three and twenty-four hours following irradiation. No appreciable differences between irradiated and control areas were observed in the diffusion of the dye into and its retention in the tissues.

EXPERIMENT VIII.—While it has been repeatedly shown that bacteria in vitro are highly resistant to x-rays, the following experiment was made to observe whether irradiation of the strain of *B. coli* in vitro in a medium containing rabbit serum, might indicate that one factor in reducing the severity of the *B. coli* infections may be an effect upon the organisms in the presence of the animal's serum.

Six test tubes of dextrose veal infusion broth containing 3 per cent rabbit serum were inoculated with one small loop of a twenty-four-hour broth culture of the organisms. These served as controls for six additional test tubes of similar broth inoculated from the same culture in similar manner and immediately before incubation exposed to 600 r of x-radiation. After twenty-four hours, forty-eight and seventy-two hours at 37° C., the growth was practically identical in all tubes.

DISCUSSION

In the above experiments it is shown that moderate doses of x-radiation exert a beneficial influence upon the course of pyogenic infections in the skin and subcutaneous tissues in rabbits where the virulence of the invading organism was moderate, where the numbers of bacteria injected were not excessive, and where the irradiation was given early after the bacterial injections, that is within five hours. The severity of the inflammation was reduced and healing accelerated in most instances.

Where the virulence was low and the natural course of the lesion was itself relatively brief, the beneficial effects of x-radiation were not clearly

demonstrable. Where the virulence was of moderate degree but where large numbers of bacteria were injected, no appreciable influence of irradiation upon the course of the infection could be observed.

The time of the irradiation in relation to the course of the infection appears to be of importance in that the greatest inhibitory effects upon the severity of inflammation were obtained shortly after injection of the bacteria. No beneficial influence could be observed when irradiation was given after suppuration was well established. Irregular results were obtained when the tissues were irradiated prior to bacterial invasion. In a few instances the intensity of the inflammation was more pronounced for varying periods in the irradiated lesions than in the controls in the same animal.

The literature dealing with the mechanism by which irradiation influences the course of bacterial inflammation has been greatly influenced by the observations of Heineke. The latter, published in 1903 when x-ray apparatus and methods of measurement were primitive, indicated that the lymphoid tissue was extremely radiosensitive. Deductions from these statements have been and are still repeatedly being made to explain the beneficial effects of irradiation on the assumption that widespread lymphocytic disintegration in the field liberates large amounts of antibacterial ferments. More recent observations, and to mention here only those of Maximow, have shown, however, that such leucocytic disintegration is not observed in sterile inflammatory foci treated locally by moderate doses of x-radiation. In the above studies no appreciable qualitative differences were observed between irradiated and control foci of inflammation at various intervals after twenty-four hours following irradiation. The lesions that were apparently benefited by the irradiation appeared as smaller lesions than the controls but were of identical character.

The marked interstitial edema resulting from the subcutaneous injection of croton oil was quite appreciably reduced by x-radiation as compared with control foci in the same animal. This suggests, in view of the unchanged character of the cellular exudate, that the mechanism of the action of x-radiation in reducing the severity of the inflammatory processes is, in part at least, an effect upon the capillary bed of the field, to permit a more rapid absorption of noxious substances. Whether this is a direct effect upon capillary endothelium or whether it is due to a transitory hyperemia (not grossly apparent) induced shortly after exposure to x-radiation and which of course includes an increased rate of local blood flow, cannot be stated from the evidence obtained in the above experiments.

In conclusion it might be added that the apparent reduction in size of certain neoplasma often noted after small doses of x-radiation and accompanied by prompt alleviation of local symptoms may be due to

an initial reduction in interstitial edema in a manner similar to that observed above in the inflammatory foci induced by the injection of croton oil.

SUMMARY AND CONCLUSIONS

In a series of experiments based upon 105 rabbits and in which non-irradiated control lesions were produced in every instance in the same animal that bore irradiated lesions the following conclusions are reached:

1. Moderate doses of 200 kv. x-radiation filtered by 1 mm. Cu + 1 mm. Al, i.e., 600 r, reduce the severity of acute pyogenic infections in the skin and subcutaneous tissues but do not necessarily hasten the final healing of these lesions. In a small percentage of cases the irradiated lesions healed more slowly than the controls.

2. The optimum opportunity for beneficial effects is obtained when the irradiation is given shortly after the injection of organisms (within five hours) and decreases as the suppurative phase (abscess formation) of the infection becomes more prominent. Irradiation twenty-four hours prior to bacterial injection did not inhibit the severity of the subsequent lesions; indeed, some of the lesions in such areas healed more slowly than the controls.

3. No evidence was obtained that the beneficial effects of x-radiation in inflammatory processes are due to widespread destruction of leucocytes, especially lymphocytes in the field with liberation of antibacterial ferments. In fact the exudate in the irradiated lesions was practically identical with that in the controls.

4. Evidence is presented to indicate that a factor in the mechanism of the beneficial action of irradiation is an effect upon the capillary bed of the field which results in more rapid absorption of soluble substances from the inflamed areas. This would permit of a less intense leucocytic mobilization necessary to cope with the infection.

REFERENCES

1. Desjardins, A. U.: Radiotherapy for Inflammatory Conditions, J. A. M. A. **96**: 401, 1931.
2. Heineke, H.: Ueber die Einwirkung d. Roentgenstrahl. auf Tiere, München. med. Wchnschr. **1**: 2090, 1903.
3. Lacassagne, A., and Vinzent, R.: Actions des rayons X sur un foyer infectieux local, provoqué chez le lapin par l'injection de Streptobacillus caviae, Compt. rend. Soc. de Biol. **100**: 247, 1929.
4. Maximow, A. A.: Studies on the Changes Produced by Roentgen Rays in Inflamed Connective Tissue, J. Exper. Med. **37**: 319, 1923.
5. Motojima, R.: Experimentelle Untersuchungen über den Einfluss der Röntgenstrahlen auf den Ablauf von Entzündungen im Vergleich mit anderen physikalischen Methoden, Strahlentherapie **29**: 30, 1928.
6. Proto, M.: L'azione dei raggi X nelle inflammazioni da germi piogeni., Morgagni **75**: 1111, 1933.
7. Schaefer, W.: Experimentelle Untersuchungen über die Wirkung der Röntgenstrahlen auf bakterielle Entzündungen, Strahlentherapie **25**: 370, 1927.

Editorials

The Appendicitis Problem

I. PELVIC APPENDICITIS

FROM various reports of studies of cases of acute appendicitis, the "typical" history is obtained in from 50 to 60 per cent of the cases. In our study the incidence is 53 per cent of 1,465 cases in which we regard our clinical data as reliable and complete. By "typical" history I mean the usual fourth-year medical student's reply and the average doctor's conception when asked to give a clinical and laboratory picture of acute appendicitis—severe epigastric pain gradually localizing in the lower right quadrant, nausea, vomiting, constipation, mild fever, leucocytosis, and tenderness at McBurney's point. When I give a student a grade of 55 per cent for such a reply, he is astounded, for the picture of the disease he has presented is emphasized in all of his textbooks. Likewise, when a practitioner is told that his patient has peritonitis from a ruptured appendix, he is frequently amazed because "the pain was general and mild; there was no nausea or vomiting; the temperature was normal, or only slightly elevated; and there was diarrhea and rectal tenesmus." When I reply to the student that the clinical picture of acute appendicitis is as varied as is the position of the appendix in human beings and that his description fits accurately only 50 to 60 per cent of the cases, he usually will find out what I mean if he wants to get a passing grade. When I tell the practitioner that what we are observing together occurs not infrequently in a study of a large series of acute cases, it may or may not do some good.

The failure to recognize acute pelvic appendicitis is a serious and often a costly diagnostic error. I readily recognize the difficulty of making a correct diagnosis, but I do believe that an awareness of certain fairly constant characteristics of this condition will materially reduce the incidence of mistakes.

The abdominal pain tends to be mild and often amounts to no more than a "discomfort." It may be confined to the lower half of the abdomen, but usually it is not localized by the patient to one side or the other. More often than not there is no vomiting and frequently there is not even any nausea. The story of tenesmus and frequent bowel movements (usually interpreted as diarrhea) serves to convince

the doctor that the correct diagnosis is an intestinal upset. So convinced is he that a white blood count and a rectal examination are not usually made. I have seen many children and quite a few adults allowed to play or work until actual perforation of the appendix takes place.

On physical examination there is general abdominal tenderness, usually more marked in the lower half of the abdomen. Muscle spasm is frequently absent or not detected. The point of maximum tenderness may be in the midline between the umbilicus and symphysis, or even on the left side.

Failure to make a rectal examination is often responsible for the error in diagnosis. In our series of 1,465 acute cases of appendicitis in which we regard the clinical data as accurate, there was rectal tenderness in 655 cases, or 44 per cent of the series.

Failure to consider seriously appendicitis in the face of such a mild story and indefinite physical findings (without doing a rectal examination or white blood count) is the commonest cause of missing the diagnosis. Students and doctors should realize that the clinical picture as outlined is most often the typical picture of acute pelvic appendicitis.

II. ACUTE RETROCECAL APPENDICITIS

Here again the mildness of the symptoms may be misleading to both the patient and the doctor. All too frequently the patient and the family are not enough concerned to seek medical advice; consequently, it is the retrocecal appendix which yields such a high percentage of appendical abscesses. The appendix being buried and protected, a free rupture of it, with generalized peritonitis, is rather uncommon. It is a frequent occurrence in a large general hospital for people, after a few days of abdominal discomfort, to leave work and walk into the institution with an obvious appendical abscess.

Even when medical advice is sought early there is often a great temptation for the doctor to be misled by the mildness of the symptoms, although acute appendicitis may be recognized or suspected; frequently it is difficult to make the patient take the situation seriously enough to consider operation. The pain may be insignificant; nausea and vomiting may be absent. Personally I do not believe in observing any cases of early acute appendicitis, for I do not consider it possible to predict with any certainty what may happen. If I should have to do it, I would much prefer "watching" a case where the appendix is free and irritating moving peritoneum and causing violent, typical textbook symptoms and signs than a case where the appendix is hidden retrocecally in a quiet spot and giving very mild symptoms and signs. It can be just as bad as, or worse than, the free appendix

giving the classical picture. I have long since refused to take the responsibility of "observing" any case of acute appendicitis and especially the retrocecal case. In my practice it must be borne by the patient or his family.

On careful physical examination, the diagnosis is usually not so difficult as in the case of acute pelvic appendicitis. Muscle spasm may be lacking, but localized tenderness somewhat above McBurney's point, or even in the flank, is present. This is usually supported by a low fever and a high leucocyte count.

III. RUPTURED APPENDICITIS

The recent advocation of the conservative treatment for cases of appendical abscess and peritonitis is having a somewhat unfortunate effect in that it is being misinterpreted alike by some laymen and doctors. It is not unusual for me to meet laymen and medical men who ask about the new treatment of acute appendicitis without operating. This growing impression may be productive of great harm and should be combated in every way possible.

I must admit some difficulty in deciding what cases of ruptured appendicitis should be treated conservatively without operating. Prior to the onset of abdominal distention in cases of general peritonitis I still believe it wise to remove the appendix through a small McBurney incision and to drain or not, depending upon the amount of contact necrosis and peritoneal soiling with fecal contents. In cases of walled-off abscesses it may often be good judgment to observe the trend of the process before deciding what to do.

Yet the value of this conservative therapy, where definitely indicated, may become dubious or harmful if its misapplication in cases of acute unruptured appendicitis should increase. It is conceivable that the total mortality from acute appendicitis may increase unless the entire medical profession (not just surgeons) should learn the clear indications for the conservative therapy and that it has no place in the management of the acute unruptured cases. Time alone will have to prove the value of its revival. I trust that it will not eventually have the effect of increasing the total death rate from appendicitis in this country.

IV. THE MEDICAL PROFESSION AND THE PUBLIC

Mistakes in the diagnosis of appendicitis are inevitable. The following remarks, therefore, are applicable only to the doctors who deliberately choose a policy of delay or nonoperative therapy when they believe the diagnosis of acute unruptured appendicitis is correct or even most likely.

In an effort to reduce the appalling death rate from appendicitis in this country, the emphasis has been put upon certain factors which appear to be definitely contributing to it. Of these, the lapse of time between onset of symptoms and operation appears to be most important. In cities where this average time is the shortest, the death rate is the lowest. For example, in Philadelphia where it is 49 hours, the death rate is 11 per 100,000 population; whereas, in Cincinnati where it is 91.2 hours, the death rate is over 30 per 100,000 population. Statistics show that the taking of purgatives by the patient or the prescribing of them by the doctor definitely increases the mortality. There are other less important factors, such as the type of operation, the handling of cases of ruptured appendicitis, etc., about which there may be some differences of opinion, but the first two mentioned are liked by the medical profession because the responsibility for the delay and the taking of purgatives can be and is being shifted directly upon the public. In communities where intensive campaigns have been conducted to educate the public with respect to the dangers of delaying operation or of taking purgatives, the mortality has been markedly reduced and doctors have been forced by public sentiment to adopt the policy of advising immediate surgical consultation for acute unruptured appendicitis.

I frequently wonder if it is right or best for the profession to sit calmly and wait for an enlightened public opinion to correct its own responsibility in the matter. Nearly every surgeon in this country knows that there are some members of our medical profession who believe in and practice the nonoperative treatment of acute appendicitis, others who counsel delaying operation until the acute attack of appendicitis has subsided. The surgeon also knows that placing the responsibility for a ruptured appendicitis squarely upon the shoulders of the doctor who has been treating a patient since the onset of the trouble brings a severance of professional relations and a countercharge of being unethical, should he be indiscreet enough to speak about it to the family or anyone else. The next time another surgeon will be called into consultation. In a recent clinic for my students in which I showed cases of ruptured appendicitis with generalized peritonitis, I read letters from two doctors who said that they had been treating two of the patients for from five days to a week and had come to the conclusion that they would not get well without an operation. I was congratulated for my bravery but warned as to the ethics of reading such letters, even though the names of the doctors were not divulged. Such letters frequently accompany patients who are sent to a large charity hospital. Furthermore, a health survey shows that in Cincinnati during the seven years prior to 1936, 300 people died in their homes from ruptured appendicitis without the benefit of surgery.

The whole-hearted support of educational campaigns in the press, in paid advertisements, in our public schools, and through radio programs and lectures would indicate a unanimous agreement among the medical profession regarding the advisability of early operation for acute unruptured appendicitis. Yet there are doctors among our profession who do not follow this policy. Should organized medicine continue, by its silence, to recognize that, after all, their opinion may be right, that in this problem of appendicitis they are a law unto themselves, and that no matter what may happen they are to be protected by a strict code of medical ethics? If so, then there is nothing to be done about the matter except to wait for the pressure of public sentiment to correct a fault in our own ranks, for individual efforts among ourselves, as pointed out, will not do it.

When certain procedures and rules are accepted as right, then there is usually some method of chastising those responsible who refuse to obey them. This is true if a doctor refuses to use antitoxin for diphtheria. It would certainly be true if a locomotive engineer chose to drive his train on the wrong track and caused the death of a number of people in a wreck. Organized medicine's sponsorship of campaigns to reduce the mortality of acute appendicitis certainly justifies the assumption that there are certain rules and regulations concerning its treatment which are right. When will organized medicine assume some responsibility for censuring those doctors who refuse to obey them? Until it does, the public will continue to pay the price of an unnecessarily high death rate while professional ethics effectively defend the offenders in our own profession.

—*Mont R. Reid, M.D.*
Cincinnati, Ohio.

Sinus Tracts and Their Identification

ONE of the most perplexing situations that confronts a surgeon is to have a patient return with a recurrence of the sinus in the identical area from which the surgeon previously has removed it. Therefore, the identification of sinus tracts and their ramifications is of paramount importance from a surgical standpoint.

Sinus formations are of two types, the congenital and the acquired; the latter type predominates. The congenital forms are the result of embryonic deviation from normal development. There are many areas in the body in which these identical sinuses occur. The most frequent sites are the neck, the umbilicus, and the sacrococcygeal region. The sinuses in the neck are associated with the branchial apparatus and form the pre-auricular, thyroglossal, and cervical sinuses, and these are very difficult to completely ablate because they are the most complicated

form. Those at the umbilicus are associated with the gastrointestinal tract and bladder, while those in the sacrococcygeal region (pilonidal sinuses) are associated with the development of the caudal end of the medullary canal. The first and last types are the most common.

The acquired types of sinus are very common and usually result from infections which drain to the surface spontaneously or which have been drained surgically. The acquired type will not be enumerated here, because they are familiar to all surgeons. However, their total removal is beset with the same difficulties that occur in the congenital types; that is, the inability to distinguish at operation the abnormal from the normal tissue. This results in a rather high incidence of recurrence.

Therefore, a successful removal of all of the sinus and its ramifications, which will prevent a recurrence, involves two principles: (1) to determine the direction and extent preoperatively and (2) to visualize the tract at operation.

The first is easily determined roentgenographically by injecting the sinus tract with an opaque substance. Lipiodol for these injections has been found to be an ideal opaque medium. Because of its fluidity, it penetrates the remotest parts of the sinus and gives excellent contrast. By means of this, the direction of the sinus tract and all of its ramifications is visualized. This visualization gives the surgeon an idea of the type of incision and predetermines the extent of the necessary dissection. Even with the aid of the roentgenogram before him, however, the surgeon often fails to remove completely the sinus tract because it frequently blends with the normal tissue.

It becomes necessary to visualize the sinus tract at operation for successful removal. This visualization is produced by staining with a dye of methylene blue. Staining the sinus tract with a solution of methylene blue is a procedure commonly used throughout the world, but the results have been anything but encouraging. This failure is due to a faulty technique. The usual technique is to inject the sinus at the time of the operation. The dye solution stains the tract blue, which should easily demarcate it from the normal tissue; but, because the dye is injected at the time of the operation, the entire field becomes stained and delineation is completely lost. This is due to the dye solution's completely filling the sinus and when dissection is started pressure is exerted on the sinus tract, emptying the dye solution from the sinus into the wound and surrounding tissues. To overcome this difficulty, we have used the following method of staining the sinus tract, which has given us very satisfactory results.

The technique as used in our clinic is as follows: Five days before the operation, we begin to stain the sinus tract with a solution of methylene blue. The sinus tract is injected under slight pressure with

the methylene solution daily for three days, then two days are allowed to elapse before the operation. This elapse of two days allows the solution to drain off and the sinus tract to dry, which results in a deeply stained tract. The "drying-out" process prevents the solution from spilling into and on the wound surfaces. This method facilitates a thorough and complete dissection of the sinus tract. One can easily differentiate at all stages of the operation the stained tract from the unstained tissues from which it is being dissected.

We have used this method for several years with most gratifying results. That the sinus tracts have been completely removed and permanent relief obtained is evinced by the absence of recurrences.

—*Mims Gage, M.D.*
New Orleans, La.

Recent Advances in Surgery

Conducted by Alfred Blalock, M.D.

ACUTE ULCER OF THE DUODENUM (CURLING'S ULCER) AS A COMPLICATION OF BURNS; RELATION TO SEPSIS

Report of a Case With a Study of 107 Cases Collected From the Literature, 94 With Necropsy, 13 With Recovery; Experimental Studies

Henry N. Harkins, M.D., Ph.D., Chicago, Ill.

(From the Douglas Smith Foundation and the Department of Surgery, University of Chicago)

THE occurrence of ulceration of the intestinal tract following burns has been recognized for one hundred years. Curling's[1] comprehensive report of 10 cases, including 4 of his own, in 1842 directed especial attention to this subject. Curling's report concerned ulcers of the duodenum only and the lesion was sufficiently common for his own 4 cases to be seen at the London Hospital in the nineteen-month period beginning in September, 1840.

HISTORICAL

Moynihan,[2] 1912, stated that unquestionably the priority should go to Long,[3] 1840, whom Curling quoted. If this is true, the same applies to Cooper,[4] 1839, whom Curling also quoted and even more so to previous authors who are not quoted by Curling or by Moynihan either. Swan,[5] 1823, reported a case with ulcers of the stomach following burns. Cumin's report[6] in the same year, which is more frequently quoted, described inflammation only. Mac Farlane,[7] 1833, is quoted as reporting cases, yet when this article is examined in the original it is seen that the report of 3 cases was in the form of editorial notes to his paper by Johnson. Dupuytren,[8] 1833, reported a case of ulcers of the stomach and duodenum following burns and in 1839 Cooper[4] reported his 3 cases of duodenal ulcer following burns, 2 of which were later quoted by Curling. In 1840 Long reported 2 cases of duodenal ulcer following burns he saw while house surgeon at the Liverpool Infirmary. Then came Curling's collected series in 1842 and numerous other case reports followed. An excellent review of the etiology of the so-called Curling's ulcer was made by Pack,[9] 1926. Collected series of cases are shown in Table I. Thiele's collection[14] is the only one since

Received for publication, Feb. 5, 1938.

TABLE I

COLLECTED SERIES OF CASES OF GASTRIC AND DUODENAL ULCER FOLLOWING BURNS

AUTHOR	YEAR	NUMBER OF CASES
Curling[1]	1842	10
Holmes and Hulke[10]	1883	16
Schjerning[11]	1884	19
Perry and Shaw[12]	1894	29
Collin[13]	1894	38
Thiele[14]	1919	31

1894 and is far from complete. The lack of any complete review in the past forty-five years was one of the stimuli for the preparation of the present paper.

FREQUENCY

The frequency of duodenal ulcers following burns is difficult to estimate from statistics as several factors of error enter in. The first and most obvious error is that some reports are based on collected reports. Thus, the oft-quoted statistics of Holmes and Hulke,[10] 1883, that duodenal ulcers occur in 12.8 per cent of cases following burns (16 out of 125 cases) is based upon the compiled records of several authors, including Curling,[1] Long,[3] and Erichsen.[15] Of the total, 75 were a series of necropsied burns seen at St. George's Hospital, London, of which 2 presented ulcers. This percentage of only 2.7 is probably much nearer the truth than the figure of 12.8 per cent. Other reports of collected statistics are 20 per cent (Birch-Hirschfeld, cited by Kaufmann,[16] 1929, who could not confirm this high figure and believed the true value was nearer 3 per cent); 6.2 per cent (Fenwick and Fenwick,[17] 1900); and 12 per cent (Erichsen,[15] 1843). Collin,[13] 1894, found that 38 of a series of duodenal ulcers were due to burns. Schjerning,[11] 1884, saw no cases himself in 63 burn necropsies, but he collected 19 from the literature. His statistics that 19.5 per cent of cases dying more than forty-eight hours after burns and 12.4 per cent of all burn deaths develop ulcers of the duodenum were based on collected statistics and disagree with his own experience. Thiele,[14] 1919, in a study of 248 ulcers in patients under 16 years of age (119 of the stomach, 185 of the duodenum; 89 boys, 98 girls) found 31 were due to burns.

A second factor of error is that patients who die within the first few hours after a burn are usually, and rightly so, not suspected of having duodenal ulcers and are not necropsied. Wilks,[18] 1856, pointed this out and Perry and Shaw,[12] 1894, stated that at Guy's Hospital "it has not been usual to inspect the bodies of patients dying of burns unless they survive the injury for several days." The omission of such cases from the statistics is thus deceiving. On the other hand, while these two factors tend to make the reported percentage higher than the true one, a third factor may work the other way. This factor

is that no statistics are available as to the percentage of ulcers following burns that go on to recovery. As discussed in the section on that subject, only within the past ten years have many such cases been reported and no gastrointestinal Roentgen study of a large series of burned patients has ever been made.

Numerous authors with a wide necropsy experience have never seen duodenal ulcer following burns. Thus Wilks,[18] 1856, in 12 necropsies following burns never saw a case. He pointed out that the difference in frequency must be a real one as it is "as equally impossible for a healthy surface to be mistaken for an ulcerated one as it is for an ulcer to appear as a smooth healthy surface." Hunter,[19] 1890; Fayrer;[20] Falk,[21] 1871; Dohrn,[22] 1901 (in 9 burn necropsies); Reuter;[23] Versé;[23] Dietrich;[23] Fahr;[23] Bardeen,[24] 1897, 1898 (in 5 burn necropsies); Moynihan,[2] 1912; Fraenkel,[25] 1898 (in 34 burn necropsies in nine years); and Marchand,[26] 1913 (in 47 burn necropsies) never saw a case of ulcer of the duodenum. The rarity of these ulcers was mentioned by Brunner,[27] 1903; Fenwick,[28] 1897; Cutler,[29] 1904; and Chiari,[23] 1914. Ewald,[30] 1912, stated that the relation between duodenal ulcer and burns is very problematical. Maes,[31] 1930, in reporting the only case seen at the Tuoro Infirmary, stated that not a single case had been seen at the Charity Hospital, New Orleans, which has one of the largest accident services in the South.

With these factors kept in mind, the data shown in Table II must be interpreted with caution. Hewett found that 3 others in his series had

TABLE II

PERCENTAGE OF DUODENAL AND GASTRIC ULCERATION FOLLOWING BURNS IN NECROPSIED CASES

AUTHOR	NUMBER OF DEATHS DUE TO BURNS	NUMBER OF ULCERS	PERCENTAGE INCIDENCE OF ULCERS
Long,[3] 1840	24	2	8.2
Curling,[1] 1842	11	4	36.4
Hewett,[32] 1848	17	3	17.7
Erichsen,[33] 1895	94	2	2.1
Simmonds,[34] 1898	50	2	4.0
Gruber,[35] 1913 (Strassburg)	22	3	13.6
Gruber, 1913 (Munich)	19	0	0.0
Stewart,[36] 1923	115	2	1.7
Ronchese,[37] 1924	34	1	2.3
Harris,[38] 1929	138	1	0.7
Riehl,[39] 1930	152	5	3.3
Author, 1937	4	1	25.0
Total or average	680	26	3.8

congestion of the duodenum, and 3 who lived beyond three weeks showed no intestinal pathology, as did 8 who died shortly after the burn. Stewart's data were based on 6,800 consecutive necropsies at the Leeds General Infirmary, and 57 patients of the 115 deaths from burns were 20 years of age or older. Ronchese's data were based on

a series of 348 burns. Harris' data were based on 567 cases of burns seen at the Toronto Children's Hospital in twelve years. Brinkman,[40] 1915, studied 10,384 consecutive necropsies performed at Kiel from 1890 to 1904 with 752 gastric ulcers, all in patients over 14 years of age. Five of these were due to burns. Willems and Kuhn,[41] 1936, reported 1 ulcer in a series of 1,206 burns, but as many of these were of very minor degree this has little statistical value.

The average incidence of 3.8 per cent agrees fairly well with the conclusion of Perry and Shaw,[12] 1894. These authors reported that of patients dying of all causes 0.4 per cent showed duodenal ulceration and no less than 3.3 per cent of those dying of burns exhibited this condition. The laws of probabilities would rule out coincidence when it is realized that a fair proportion of these ulcers causes death by hemorrhage or perforation within three weeks following the burn. If the incidence of 3.8 per cent of Curling's ulcers applies to the entire group of 6,000 persons that lose their lives annually in the United States from burns, this would mean a total of over 200 instances of fatality with Curling's ulcer per annum in this country. However, many of the 6,000 cases die very soon after the burn and cannot be included. At least, the number is probably higher than commonly realized.

ETIOLOGY

Ulcers of the duodenum are of such rarity that no one author has seen a large series with the exception of some of the earlier writers and these were interpreted without the benefits of the modern viewpoint. The exact mechanism of formation of the ulcer is as yet unknown, but there are almost as many theories as observers. A few of these will be listed below:

1. *Compensatory Hypertrophy of Brunner's Glands.*—Curling,[1] 1842, believed that these glands sympathized and compensated for the suppression of skin exhalation by an increased activity. This, in turn, led to an irritation which caused inflammation and ulceration. In support of this theory was the finding of hypertrophy of these glands in occasional cases by Curling and others. Fourcault, Gluge, Gerlach, Ducros, Magendie, Becquerel, Breschet, and Balbiani[42] believed that interference with skin secretions caused internal congestion. However, many of the reported ulcers following burns occurred after burning of only a relatively small area of skin. Fenwick and Fenwick,[17] 1900, believed that interference with the natural excretion of the skin, just as in nephritis, will give duodenitis. They performed experiments as follows: a water-alcohol extract of burn sloughs gave a white powder like an albumose. This, when injected subcutaneously in a rabbit or cat, gave an appreciable degree of duodenitis. The gaps between these experiments and the authors' conclusions are difficult to bridge.

2. *The Antiferments of the Mucous Cells Are Reflexly Destroyed.*—Cooke.[43]

3. *Excessive Gastric Acidity.*—Wilson,[44] 1935, has shown by gastric analyses in burns of similar extent that there is no excessive gastric acidity.

4. *Secondary to Hypothalamic Lesion.*—Wilson,[44] 1935, searched for such a lesion in one of his cases with negative results.

5. *Direct Action of Heat on Intestines.*—Underhill, Kapsinow, and Fisk,[45] 1930. These authors measured the intraabdominal temperature in rabbits experimentally burned on the abdomen. In several instances the intra-abdominal temperature exceeded 110° F. when the rectal temperature remained near normal. They stated that most of the macroscopic changes characteristic of burns have been noted in their experimental animals. This, however, was true only when the heat penetrated the abdominal cavity. If the burn was remote from this region nothing abnormal was ever noted except for some congestion. Opposed to this theory is the observation that many Curling's ulcers occur when the burn spares the abdomen. In the present series of 52 cases with data sufficient for analysis, in 29 cases the abdomen was not burned. Wilson,[44] 1935, stated "the suggestion that the direct action of heat on the viscus might produce the ulcers need not seriously be entertained." I have performed experiments which show that a more protracted application of heat than occurs in many clinical cases is necessary to raise the intra-abdominal temperature to the degree reported by Underhill, Kapsinow, and Fisk.

6. *Reflex Inhibition of Intestinal Circulation.*[9]

7. *Inflammation.*—Gibbon,[46] 1855. Contrary to the theory just mentioned, this author believes the ulcers are due to inflammation which attacks the duodenum because it is one of the most vascular of organs.

8. *Spinal Reflex From Burned Skin.*—Brown-Séquard,[47] 1858. This author believed that if the reflex arc were broken, ulcers could not occur. He stated: "In two cases, on animals on which the trunks of the sciatic and crural nerves in one limb had been divided as high as possible, I have not found a state of marked congestion of any viscus, three days after I had carbonized this limb from the toes to the middle of the thigh. From these experiments and the preceding, it results that it is, in a great measure, by a reflex action of the spinal cord, that burns produce their deadly influence on the viscera." Burning of the hindlegs with lumbar cord section prevented visceral congestion likewise, but section at the third dorsal region did not prevent visceral congestion. This work refers to congestion rather than ulcers and all of Brown-Séquard's animals were killed on the third day, long before most Curling ulcers in human beings develop.

9. *An Inhibition of Gastrointestinal Circulation Results From a Depressed Action of the Heart.*—Or it results from impaired nourishment of the mucous membrane (Falk,[21] 1871).

10. *An Inhibition in the Force of the Circulation Results From Accumulation of Waste Products in the Blood.*—Leube.[48]

11. *A Toxin Reaching the Intestinal Wall Causes a Reduction in Its Natural Alkalinity, Allowing Digestion of the Mucosa to Ensue.*—Catiano,[49] 1882.

12. *Irritant Action of Noxious Bile.*—Mendel,[50] 1870, believed that a pathologic modification of the bile with resultant inflammation was a factor. Hunter,[19] 1890, attributed the ulcers to the action of noxious bile. The bile was supposed to give its injurious effects due to its content of the presumptive burn toxin, secreted by the liver. This author produced ulcers experimentally in dogs usually at least six inches below the pylorus by the subcutaneous injection of toluylidiamine. Fenwick and Fenwick,[17] 1900, repeated these injection experiments after ligation of the common bile duct. In one instance two perforating ulcers of the duodenum resulted which would tend to cast doubt on Hunter's conclusions.

13. *Action of Burn Toxin.*—This theory differs from the preceding in that it assumes that the toxin is carried to the intestine by the blood stream rather than by way of the bile. Maes,[31] 1930, states: "The consensus of modern opinion regards the toxemia of burns rather than the circulatory disturbances as responsible for the production of the associated duodenal ulcers." Harris,[38] 1929, believed that the "action of the toxin produces focal necrosis and hemorrhage in the duodenal mucosa, and that these areas are transformed into ulcers by the digestive action of the pancreatic juice." Dohrn,[22] 1901; Sherren,[51] 1923; and Wells,[52] 1925, also ascribed to the toxic theory.

14. *Absence of Biliary Secretion.*—Pack and Davis,[53] 1930. This is quite opposite to Theory 12. These authors quote the work of various writers who showed that if the biliary flow is diverted from the duodenum, ulcers of this structure may develop. They postulated that, because of the marked blood concentration attending severe burns, the bile may become so inspissated that it does not flow readily.

15. *Stasis Due to Blood Concentration.*—Kapsinow,[54] 1934. This author believed that rupture of the capillaries underlying the duodenal mucosa producing an inefficient oxygen supply to the tissues with necrosis of the mucosa was the causative factor.

16. *Stasis Due to Low Blood Volume.*—The decreased blood volume in severely burned animals is well known.[55, 56] Brooks and Blalock,[57] 1934, produced a low blood volume by very gradual hemorrhage and found in their dogs at necropsy necrosis, capillary congestion, and hemorrhage in the duodenum and necrosis and congestion in the adrenal glands.

17. *Nervous Influences Because of Proximity to Great Sympathetic Plexuses.*—Paget,[58] 1890.

18. *"Shock" to the Stomach.*—Since shock exists in burns, Hills,[59] 1881.

19. *The Action of Toxins Plus Gastric Hyperacidity Due to Shock.*—Levin,[60] 1929.

20. *Stasis in a Circumscribed Zone.*—Kraus,[61] 1863; Klebs,[61] 1869; and Jez,[61] 1900, all attributed the ulcers to stasis in a circumscribed zone with secondary digestion.

21. *Autodigestion.*—Ponfick,[62] 1876.

22. *Capillary Thrombosis.*—Sonnenburg,[63] 1879; Leotta,[63] 1904; and Ewald,[63] 1912.

23. *Hydrocyanic Acid.*—Catiano,[49] 1882.

24. *Fat Embolism.*—Salvioli,[64] 1891; Merkel,[65] 1914.

25. *Fatty Degeneration, Similar to Lead Poisoning.*—Cassanello,[66] 1921.

26. *Adrenal Theory.*—The experimental work of Mc Laughlin,[67] 1933, on the production of graduated adrenal damage in dogs with resultant ulcer formation is of interest. The partial destruction of the adrenal glands was not sufficiently extensive to cause gross adrenal insufficiency. In a series of 21 dogs, 17 showed definite ulceration of the small bowel, but in no instance was ulceration seen in the stomach. Three cases in the present series had adrenal hemorrhages, those of Harris,[38] 1929 (Case 78); Riehl,[39] 1930 (Case 86); and Harkins, 1937 (Case 94). Since some of these had focal lesions in so many organs, it is difficult to state that one is cause and the other effect. The absence of reported adrenal damage in the other 91 cases of duodenal ulcer following burns indicates that the relation may be concomitant rather than causal. Furthermore, several instances[72] of adrenal change following burns without associated Curling's ulcer have been reported.

27. *Embolic Theory.*—Billroth,[68] 1867, was one of the first to attribute the ulcers to an embolic process. He believed that the infarcted area sloughed away. Fenwick and Fenwick,[17] 1900, in opposition to the embolic theory, point out that emboli do not generally attack the stomach and duodenum and, if they do, embolism of the duodenum never occurs without embolism of the stomach. They also state that in no case was the obstructed vessel ever found. Case 53 of the present series is an exception to this last statement. Ponfick,[62] 1876, also discussed the relation of these ulcers to infarction. Broadbent,[69] 1908, stated, concerning these ulcers, that "the most plausible [explanation] would seem to be that the congested condition of the intestines is the predisposing, and septic embolism or thrombosis of a small vessel fol-

lowed by digestion of the necrotic area the determining cause." Stengel,[70] 1926, reported that recent studies tended to support the theory of embolism with secondary digestion.

Erichsen,[33] 1895, opposed the idea of Curling that the ulceration begins in Brunner's glands and stated: "It is far more probable that it is due to the acid contents of the intestine acting on a point in the mucous membrane in which a capillary embolism has lodged." He pointed out that in favor of this view are the facts that the ulceration occurs at the time the burned area is sloughing; that the ulceration is at the beginning of the duodenum, "before the contents of the bowel have been neutralized by the bile"; that acute inflammation in the region of the ulcer is usually not present; and that similar ulceration has been reported in cases of septicemia not caused by a burn. Moynihan,[2] 1912, noted that the ulcers usually occurred when the burned area was undergoing septic changes and believed that septic emboli were the cause.

28. *Septic Theory.*—The frequent association of infection in the burned area with subsequent development of a duodenal ulcer has been repeatedly noted. That such an infection may act by way of an embolic phenomenon has just been discussed. It may also act by means of toxin production which acts directly upon the duodenum. Such a toxin also could act conceivably upon the adrenals, this in turn producing the duodenal changes; or the adrenal changes may be purely concomitant. The recent reports of Aldrich,[71] and others[72] on the importance of infection in the morbidity and mortality following burns are quite apt in this connection. Billroth,[68] 1867, was one of the first to notice the connection between sepsis following thermal injuries and duodenal ulcers.

The case of Greenwood,[73] 1880, is frequently quoted as an instance of Curling's ulcer, but it is really more an example of ulcer secondary to sepsis. A man, aged 40 years, had an amputation for an infected carcinoma of the penis. Secondary hemorrhage developed in the sloughing wound that resulted. Hot water was used to stop the hemorrhage, with resultant blistering. The wound remained infected; the temperature was 105.8° F.; the pulse, 148; and the patient died in four days with the finding of a perforated ulcer of the duodenum.

The frequency of duodenal ulcer following burns of the abdominal wall has been explained by Stallard and Borman[74] as due to the passage of septic emboli from the burned surface, by way of the vascular or lymphatic channels in the ligamentum teres, to produce infarction in the duodenal wall. This theory only explains those cases where the abdominal wall is burned and, as mentioned in the discussion of theory 5, an abdominal wall burn is not invariably found in the cases of duodenal ulcer secondary to burns.

Melchior,[75] 1911, calls them septic ulcers and quotes Simmonds as noting a decreased frequency in the postantiseptic era. Hertz and Digby,[76] 1913, say: "It seems that in recent years the frequency of the association [of duodenal ulcer with burns] has diminished, possibly owing to the improved treatment of burns resulting in the less frequent occurrence of septic infection."

Stewart,[36] 1923, in discussing acute peptic ulcer says that one-half of them were due to sepsis and states that "bacterial infection and intoxication is, however, undoubtedly the most important direct cause of acute gastric and duodenal ulcer." He goes on to say that ulcer following burns was less frequent than formerly, "possibly because burns became more frequently septic." Several other authors have noted the occurrence of duodenal ulcer in other types of sepsis. Singer,[77] 1921, had 2 cases following sepsis, 8 of Rosenbach's,[78] 1912; 30 ulcers were associated with some infective process, and Collin,[13] 1894, mentions several cases of duodenal ulcer secondary to sepsis.

Held,[79] 1923, also attributed these ulcers to sepsis and Wilson,[44] 1935, stated that severe infection of a large area of deeply burned tissue is a common association with Curling's ulcer. One of the most extensive reports favoring the septic theory is that of Perry and Shaw,[12] 1894. These authors collected 18 cases of duodenal ulcer associated with sepsis from the Guy's Hospital records and 3 from other sources. The Guy's cases gave a ratio of 18 septic ulcers to 52 from all causes and "duodenal ulceration is associated with septic conditions nearly as frequently as it is with burns. With regard to the origin of the septic processes in the twenty-one cases here collected, it is interesting to note that in ten of them there was some sloughing condition of the skin or cellular tissue. Two had sloughing bedsores, one a sloughing leg, three cellulitis, one sloughing of the scrotum, two gangrene, and one a carbuncle. . . . It is much easier to establish the existence of some relationship between septic absorption and duodenal ulceration than to explain the exact nature of the association. It is, however, a matter of common observation that in all septic processes petechiae are found widely scattered beneath serous and mucous membranes in the alimentary canal as well as elsewhere. It is, we think, to such extravasations of blood in the duodenal mucous membrane, together with the solvent action of the gastric juice, that we must look for an explanation of the ulceration. . . . The mode of production of ulcers associated with burns seems to us to be identical with that of septic ulcers, and in nearly every case it is highly probable that the septic condition of the burnt surface is indeed the direct cause of the duodenal ulcer. As bearing upon this point we find that during the fifty years in which 149 cases of burns were inspected at Guy's, 597 cases were inspected which presented some obviously septic or pyaemic

condition. Whilst in the burn group five instances of duodenal ulceration were met with, in the septic group there were sixteen such cases, the former giving a proportion of 1 to 30, the latter of 1 to 37 approximately. It is not asserted that the ulceration of the duodenum is directly caused in every case by the septic condition of the burns, but we think our numbers afford strong presumptive evidence of the general accuracy of this hypothesis. Burns are indeed, particularly liable to lead to sloughing of large tracts of skin." In many of their collected cases such sloughing was specifically mentioned as being present. Finally, in the present series in 24 instances mention was made of septic change in the burned area or of septic complications elsewhere.

Paget,[58] 1890, was an opponent of the septic theory. He stated: "In only one instance (P. Hewett) is it recorded that the raw surface of the burn took on an unhealthy action at the time when symptoms of duodenal ulceration were first observed. . . . Not one case showed true pyaemic abscesses elsewhere: nor, in most of the cases, is there record of marked signs during life of pyaemia or septicaemia." These statements are based on an incomplete study of the literature before this time as several of the present series of collected cases reported before Paget's article showed marked evidence of sepsis (Cases 29 and 31). Furthermore, all 3 of Hewett's cases[32] showed marked evidence of sloughing and in 1 the burn was so deep the tracheal rings were exposed.

REPORTED CASES

In the following 94 case abstracts all of the reported instances of duodenal or gastric ulcer following burns found in the literature are reviewed. In each abstract, if any of the following facts are not mentioned, data were not given concerning them in the original reports.

Age.—Average in 74 cases with data given on this point, 14.6 years.

Sex.—In 65 cases with data given, 47 females and 18 males.

Degree of Burn.—Third degree, 38 cases; second degree, 2 cases; first degree, 1 case.

Area Involved.—Abdomen burned in 23 of 52 cases.

Melena.—Present in 16 of 23 cases.

Vomiting.—Present in 26 of 31 cases.

Hematemesis.—Present in 13 of 22 cases.

Length of Life After Burn.—Average, 15.4 days in 68 cases.

Sudden Onset of Symptoms.—Present in 19 of 44 cases.

Location of Ulcers.—Duodenum alone, 71; stomach alone, 16; both duodenum and stomach, 5.

Number of Ulcers.—Single, 57 times; multiple, 34 times.

Perforation.—Present in 14 of 49 cases.

Hemorrhage.—Present in 27 of 42 cases.

Sepsis.—Present in 24 of 24 cases.
Pancreas Exposed.—In 18 of 38 cases.
Pancreaticoduodenal Artery Eroded.—In 13 of 36 cases.

CASE 1.—Swan,[5] 1823: A boy, aged 5 years, was burned, including part of the epigastrium. He received oil treatment, vomited, and died in forty-eight hours. "On opening the abdomen, every part appeared sound except the stomach in the villous coat of which were several spots and stripes like sloughs, extending deep, and quite black."

CASE 2.—Dupuytren,[8] 1833: A woman, aged 27 years, died thirty-six hours after a burn. In the stomach and near the pylorus were numerous small ulcerations.

CASE 3.—Johnson,[7] 1833: "The majority of those whom we have seen die, at any distance of time after the infliction of the burn, have certainly sunk from ulceration of the intestinal mucous membrane. We lately saw a remarkable instance of perforation of the stomach, in consequence of an ulcer which began in its mucous coat." Hematemesis and melena occurred before sudden death between the second and third week. At necropsy, ulcers were present in the stomach, 1 of which had perforated, and in the terminal ileum.

CASE 4.—Johnson,[7] 1833: "In another case of death after burn we saw similar ulcerations of the stomach, unattended with perforation."

CASE 5.—Johnson,[7] 1833: A girl died ten to fourteen days after a burn with extensive ulcerations of the mucous membrane of the stomach and intestines.

CASE 6.—Cooper,[4] 1839: Mary W., aged 3 years, was admitted to the University College Hospital with extensive burns of the abdomen, chest, arms, and occiput. Flour dressings were applied. Vomiting occurred throughout the course, at first of dark brown material and then of blood the day before death on the fifth day with convulsions. A large perforating ulcer of the duodenum with peritonitis and blood in both intestines and peritoneal cavity were found. There were three smaller additional ulcers in the duodenum.

CASE 7.—Cooper,[4] 1839: Hannah L., aged 8 years, was admitted to University College Hospital five weeks after being scalded on the chest, and died two days later. Three weeks after the burn she began to pass blood from the rectum. At necropsy there was a 2 cm. ulcer in the duodenum with its base formed by the pancreas. There was considerable blood in the intestines. The original burn of this patient was treated with flour.

CASE 8.—Cooper,[4] 1839: Girl, aged 9 years, died four weeks after a burn that did not involve the abdomen. At necropsy an ulcer of the stomach, nearly cicatrized, was found.

CASE 9.—Long,[3] 1840: Ann. J., aged 28 years, with deep and extensive burns, vomited every day, had tenderness in the epigastrium and died on the eighth day. A perforated ulcer of the superior angle of the duodenum, 2 cm. in diameter, tamponaded by the gall bladder and without peritonitis, and two or three smaller duodenal ulcers were found at necropsy.

CASE 10.—Long,[3] 1840: Helena B., aged 14 years, complained of pain in the epigastric region ten days after a burn on the nates, neck, and arms. On the twelfth day she died, eleven hours after the onset of symptoms of acute peritonitis. Necropsy revealed intense peritonitis and a perforating ulcer in the duodenum near the pylorus.

CASE 11.—Curling,[1] 1842: M. A. F., girl, aged 11 years, had a profuse hematemesis the eighteenth day after a deep third degree burn of the chest and arms. Repeated hematemeses and some melena were followed by death in fifteen more hours. Necropsy revealed blood in the stomach and intestines and a half inch diametered ulcer of the duodenum an inch from the pylorus. The base of the ulcer was formed by the pancreas and the open mouth of a large vessel was seen.

CASE 12.—Curling,[1] 1842: A male child, aged 4 years, had extensive burns on the neck, chest, and arms. Thirteen days later he had pain in the abdomen and vomited one-half pint of blood. Melena occurred until death the fourteenth day in convulsions. Necropsy revealed blood in the stomach and intestines and a solitary ulcer 2 cm. in diameter in the posterior part of the duodenum. The base was formed by the pancreas and the ends of an eroded blood vessel were seen. Perforation into the peritoneal cavity had almost occurred.

CASE 13.—Curling,[1] 1842: A girl, aged 8 years, died shortly after passing blood by stool ten days after extensive third degree burns. At necropsy an ulcer in the duodenum was found, 1 by ¾ inch in size, reaching to within ¼ inch of the pylorus with its base formed by the pancreas and the eroded pancreaticoduodenal artery visible. It had almost perforated into the peritoneal cavity.

CASE 14.—Curling,[1] 1842: A boy, aged 3½ years died the eleventh day after extensive third degree burns. The stomach and duodenum only were examined. There was a duodenal ulcer an inch from the pylorus that had penetrated to but not through the serosa.

CASE 15.—Stanley,[80] 1842: A girl, aged 10 years, after getting along well following a burn was seized with extreme pain in the abdomen, vomiting and collapse on the fourteenth day, and died the next morning. At necropsy two large and several small ulcers of the duodenum were found. One of the large ulcers was tamponaded by the pancreas and the other had perforated into the general peritoneal cavity. The smaller ulcers involved the mucous membrane only.

CASE 16.—Lee,[80] 1842: Sarah T., aged 19 years, was burned on the thighs and shoulders. Death occurred the tenth day with melena and bloody vomitus the day before death. At necropsy a large clot was found in the duodenum with a single duodenal ulcer perforating into the peritoneal cavity. The perforation was closed off with fibrin. The rest of the intestines showed congestion.

CASE 17.—Lee,[80] 1842: Duodenal ulcer following a burn.

CASE 18.—Erichsen,[15] 1844: H. L., female, aged 8 years, died the tenth day after a chest scald, and at necropsy a duodenal ulcer the size of a shilling was found.

CASE 19.—Erichsen,[15] 1844: Female, aged 9 years, with a burn on the chest died on the thirtieth day. At necropsy an ulcer of the stomach that was nearly cicatrized was found.

CASE 20.—Erichsen,[15] 1844: Female, aged 5 years, burn on abdomen, death on eighth day, ulcer in duodenum an inch below pylorus found at necropsy.

CASE 21.—Erichsen,[15] 1844: Female, aged 9 years, burn on chest, death fourth day, duodenal ulcer found at necropsy.

CASE 22.—Jaksch,[81] 1844: Author has seen 2 cases of duodenal ulcer after severe burns that had all the signs of perforated gastric ulcer.

CASE 23.—Jaksch,[81] 1844: Author's other case of duodenal ulcer with perforation following burn.

CASE 24.—Luke,[82] 1844: Emily W., aged 15 years, received third degree burns of the chest, upper part of the back, neck, and left arm. There was considerable

fever for five days and pain of intermittent character in the epigastrium during the week before death on the fourteenth day. Twelve hours before death she vomited black blood and passed considerable tarry stool. A 2 cm. diametered ulcer in the duodenum 1 cm. from the pylorus exposed the pancreas and the open mouth of a large vessel. The ulcer showed beginning healing.

CASE 25.—Hewett,[32] 1848: S. C., female, aged 66 years, received third degree burns of the neck, back of trunk, arms, and right leg. The burned areas developed sloughs and the patient went into a "typhoid" state and died after seventeen days. There were no abdominal symptoms. At necropsy two ulcers of the duodenum were found. These went down to and exposed the muscle fibers. The larger ulcer was within ¼ inch of the pylorus and was 1½ by ½ inches in size.

CASE 26.—Hewett,[32] 1848: L. T., female, aged 6 years, received burns, partly third degree, of the face, neck, chest, and arms. Sloughing later exposed rings of the trachea. Diarrhea began the twelfth day, death occurred the twentieth. No melena or abdominal pain at any time. An ulcer was found in the first part of the duodenum extending down to the peritoneum over the pancreas but with no perforation.

CASE 27.—Hewett,[32] 1848: A girl, aged 6 years, was severely burned on the chest, neck, back, and left arm. There were febrile symptoms for a few days, but later she did well. On the fifty-seventh day the wounds began to slough and she had profuse sweats. She vomited from the seventy-second day until the time of death on the seventy-fifth day. There had been no pain in the abdomen or melena. Autopsy revealed nephritis and three ulcers in the first part of the duodenum. The two largest laid bare the muscular coat; the other was more superficial.

CASE 28.—Hawkins,[83] 1850: A child, aged 6 years, received burns of the arms, upper part of the body and face; and after being seemingly in a convalescent state died suddenly 4½ days after the burn. There was no melena or hematemesis. Necropsy revealed much blood in the bowel and an ulcer 3 by 2 cm. in the duodenum exposing the pancreas and an eroded branch of the pancreaticoduodenal artery.

CASE 29.—Gibbon,[46] 1855: G. C., male, aged 45 years, a candlemaker, fell into a large cistern of boiling water and scalded the lower half of his body and his hands and forearms. Blisters formed over the entire area and a zinc dressing was applied. In a week bread poultices were used because of sloughing. On the eighteenth day diarrhea and rigidity of the abdomen began. On the last three days of life before death on the sixteenth day there was fecal vomiting. Necropsy of the duodenum only revealed a very vascular mucous membrane with numerous small ulcers and two larger ones just above the ampulla extending into the muscularis only.

CASE 30.—O'Sullivan,[84] 1864: M. B., female, aged twenty-eight years, received fifth degree (Dupuytren classification) burns of the face, neck, chest, arms, and right hypochondriac region. She vomited often and died on the eleventh day. Two large ulcers were found in the duodenum adjacent to the pancreas.

CASE 31.—Curling,[85] 1866: E. R., a girl, aged 7 years, received a third degree burn over the left thigh and greater part of the abdomen. There occurred considerable sloughing of the burned area. The stools were bloody beginning the sixth day. Death occurred the eighth day and the patient cried out suddenly five hours before death. An ulcer was present in the duodenum 1 by ½ inch beginning ½ inch from the pylorus. The pancreas formed part of the base of the ulcer and the pancreaticoduodenal artery was exposed, a clot lying in the opening of the vessel. An opening was present into the free peritoneal cavity, but there was no peritonitis. It was thought that this opening probably occurred when the patient cried out in pain.

CASE 32.—Clark,[86] 1867: A girl, aged 10 years, with extensive scalds did well for fourteen days after which she began to complain of abdominal pain. This continued until the seventeenth day when signs of peritonitis set in and she died the eighteenth day. At necropsy a perforated ulcer of the duodenum near the pylorus was found

CASE 33.—Cuthbertson,[87] 1867: G. W., a boy, aged 10 years, was burned on the legs and arms only. He was treated with carron oil and nineteen days after the burn developed tenderness in the epigastrium, hematemesis, and melena; and he died within thirteen hours. In the duodenum were two ulcers, one on the anterior surface an inch from the pylorus and 1 by ½ inch in size with perforation and a smaller ulcer on the posterior surface. Death was attributed to hemorrhage.

CASE 34.—Cuthbertson,[87] 1867: Cites case of a girl who died six weeks after a burn with a duodenal ulcer that was already beginning to cicatrize.

CASE 35.—Mc Carthy,[88] 1874: A. B., a girl, aged 7 years, received severe burns of the chest and upper part of the abdomen. On the fifth day she suddenly vomited a large quantity of blood. Melena ensued and she died on the eighth day. Two ulcers in the duodenum, with the pancreas forming the base of each, were present, one near the pylorus and one near the biliary papilla.

CASE 36.—Mc Carthy,[88] 1874: Duodenal ulcer following burn.

CASE 37.—Stokes,[89] 1876: A boy, aged 18 years, fell into a fire during an epileptic fit and sustained fourth degree burns of the body, including the upper abdomen. He felt well and had an appetite until the seventeenth day when he had a severe hematemesis. He collapsed and died on the eighteenth day. A large oval ulcer in the stomach far from the pylorus, two small ulcers of the pylorus, and a large oval perforating ulcer of the duodenum were found. No peritonitis was present.

CASE 38.—Ponfick,[62] 1876: F., a man, aged 18 years, fell into hot water up to his neck for two minutes and died within eighteen hours. At necropsy small ulcers were found in the stomach and one in the duodenum. There was congestion and hemorrhage into the wall of the small and large intestines.

CASE 39.—Smith,[90] 1876: A patient died after a burn, and at necropsy three ulcers were found perforating all layers of the duodenum. No blood was found in the intestine and there was no peritonitis.

CASE 40.—Hills,[59] 1881: E. G., an epileptic girl, aged 18 years, who had previously been burned at the age of 5 years, was now scalded (fourth degree Dupuytren) on the nates, thighs, and feet. Vomiting occurred the second day and she died in eighty-three hours. A nonperforating, nonbleeding ulcer the size of a shilling two inches below the pylorus in the duodenum had exposed the pancreas. The ulcer was not believed to be the cause of death.

CASE 41.—Halla,[91] 1884: Duodenal ulcer following a burn.

CASE 42.—Welti,[92] 1889: K. R., male, aged 22 years, earlier in year had a burn on the right elbow region with resultant contracture. On April 18 he had a new burn from fireworks' explosion. Olive oil therapy was applied to a second (slight third) degree burn of the face, shoulders, and back. Two days later there was blood and albumin in the urine and a fever of 40° C. The fourteenth day after the burn there was still fever and the patient vomited twice. The fifteenth day he died. In a group on the lesser curvature of the stomach 7.5 cm. from the pylorus were six ulcers; the largest was 1 cm. in diameter. The duodenum was normal.

CASE 43.—Perry and Shaw,[12] 1894: Marion C., aged 13 years, received a third degree burn of the neck, back, buttocks, and left thigh. On admission to Guy's Hospital the fifth day, she was delirious, had a high fever, and vomited occasionally. The burn was sloughy and part of the skin hung in shreds, exposing the fat beneath. She died of tetanus the thirteenth day. At necropsy an ulcer one-third inch in diameter just beyond the pyloric ring was found. The mucous membranes of the stomach and duodenum were injected.

CASE 44.—Perry and Shaw,[12] 1894: Herbert E., aged 4 years, received severe burns upon the lower extremities and buttocks. He did well for sixteen days, after which melena occurred which proved fatal on the nineteenth day. At necropsy a duodenal ulcer, ½ inch from the pylorus, about 1½ inches long, with its base formed by the pancreas in which was the eroded superior pancreaticoduodenal artery, was found. There was much blood in the intestines.

CASE 45.—Perry and Shaw,[12] 1894: A child was admitted to Guy's Hospital because of burns of the upper half of the body in 1847. He was well until the twenty-fifth day when he became comatose. Death occurred the next day. Marked suppuration of the burned areas on the chest and neck with exposure of the occipital bone, antemortem thrombi in cerebral sinuses, and in the duodenum 1 cm. from the pylorus was a small circular ulcer going to, but not through, the serosa.

CASE 46.—Perry and Shaw,[12] 1894: William J., aged 4 years, died fifteen days after a burn. In the duodenum was a superficial ulcer ½ cm. in diameter situated 2 cm. from the pylorus.

CASE 47.—Perry and Shaw,[12] 1894: William T., aged 42 years, received an extensive scald of the extremities, face, and abdomen from a boiler explosion from which he died thirteen days later. Two small ulcers were found in the duodenum.

CASE 48.—Perry and Shaw,[12] 1894: A female child, aged 4 years, was scalded on the face, neck, chest, and arms. Melena occurred the fourth day. "In some places the skin was ulcerated, and the ulcers did not present a healthy aspect." Thirteen days after the burn she began to vomit everything she took and passed blood by the bowels, and two days later she died. Necropsy revealed several small ulcers in the upper part of the duodenum and one large ulcer on the lesser curvature. The source of the hemorrhage was not discovered.

CASE 49.—Perry and Shaw,[12] 1894: A boy, aged 7 years, was admitted to the London Hospital for extensive burns on the front and back of the body, the burns being so deep that when the sloughs separated the muscles were laid bare. Death occurred in four weeks, the patient having had no intestinal symptoms. Two ulcers, one just beyond the pylorus with penetration to the peritoneum and a smaller shallower one in the duodenum 3 cm. distally, were present.

CASE 50.—Perry and Shaw,[12] 1894: Female, aged 70 years, died on tenth day after a burn. An ulcer was present in the duodenum just distal to the pylorus, with its base formed by the muscular coat. A second superficial ulcer was present in the stomach.

CASE 51.—Fenwick,[28] 1897: A girl, aged 12 years, died seven days after severe burns of the arms and legs. A 2 cm. diametered ulcer of recent formation was present in the center of the lesser curvature of the stomach. The rest of the stomach and the duodenum were congested.

CASE 52.—Fenwick,[28] 1897: London Hospital specimen of duodenum with several small ulcers following burns.

CASE 53.—Simmonds,[34] 1898: A girl, aged 4 years, died eleven days after a burn of the upper portion of the body. There were several small ulcers and one

large ulcer in the duodenum. The latter had exposed the pancreas and eroded a small vessel with extensive bleeding. The ulcer appeared to be acute. Microscopically, at the edge of the ulcers, were numerous small vessels filled with hyaline thrombi.

CASE 54.—Simmonds,[34] 1898: Duodenal ulcer following a burn in an adult.

CASE 55.—Fenwick and Fenwick,[17] 1900: London Hospital specimen with two ulcers in the stomach and one in the duodenum following burns.

CASE 56.—Weidenfeld and Zumbusch,[93] 1905: A patient, aged 36 years, who was burned (second degree over one-third of the body surface and third degree over one-sixth) was treated daily with 4 liters of saline infusion. Death occurred the fourteenth day and at necropsy a bleeding ulcer of the stomach was found.

CASE 57.—Rosenbach,[78] 1912: A girl, aged 4 years, with third degree burns of the arms, breast, and face, died on the eleventh day. Necropsy revealed multiple duodenal ulcers with exposure of the pancreas, erosion of an artery, and associated blood in the intestines and parenchymatous nephritis.

CASE 58.—Rosenbach,[78] 1912: A boy, aged 4 years, with burns including the crotch and genitalia, died on the sixth day, and at necropsy a single large ulcer was found in the duodenum near the pylorus.

CASE 59.—Moynihan,[2] 1912: Eliz. J., aged 5 years, following a burn involving the face, neck, and arms, had pain in the abdomen but no vomiting or purging. After death on the fifth day, a large oval ulcer of the duodenum just beyond the pylorus 1½ by ½ inches with a branch of the pancreaticoduodenal artery laid bare in its base was found. Blood was found in the intestines and there was a second ulcer near the main one.

CASE 60.—Gruber,[35] 1913: A man, aged 27 years, died six days after third degree burns, and at necropsy several very small peptic ulcers were found in the duodenum.

CASE 61.—Gruber,[35] 1913: A girl, aged 5½ years, died after second degree burns and at necropsy two large ½ cm. peptic ulcers of the mucosa of the duodenum just distal to the pylorus were found.

CASE 62.—Gruber,[35] 1913: A girl, aged 4 years, died after second degree burns and at necropsy a 1 cm. diametered, sharp bordered peptic ulcer of the duodenum was found.

CASE 63.—Gruber,[35] 1913: At necropsy of a girl, aged 15 years, after a burn, numerous gastric ulcers were found.

CASE 64.—Busse,[94] 1914: A girl, aged 15 years, was burned on the upper part of the body. The fever rose to 39.8° C. and she died in six days. At necropsy ulcers were found in the region of the cardia. Two ulcers were present in the duodenum 4 cm. below the pylorus and a third smaller ulcer was present on the opposite side of the duodenum like a kissing-ulcer.

CASES 65-69.—Brinkman,[40] 1915: Five cases of ulcer of the stomach following burns.

CASE 70.—Ashby,[95] 1917: A female, aged 11 weeks, who was burned on parts of the body other than the abdomen, was treated with flour and oil. When seen two days later there was already considerable pus, vomiting, temperature of 103.4° F., and a pulse of 148. The eleventh day there were tarry stools; on the thirteenth day a right panophthalmitis was diagnosed; and on the seventeenth day the patient died. An ulcer 1.3 cm. in diameter with no perforation and no visible vessel eroded to account for the hemorrhage was found at necropsy.

CASE 71.—Mayer,[96] 1919: A girl, aged 6½ years, had hematemesis and died after a burn. A single duodenal ulcer exposing the pancreas and eroding the pancreaticoduodenal artery was found at necropsy.

CASE 72.—Singer,[77] 1921: Duodenal ulcer following burn found at necropsy.

CASE 73.—Singer,[77] 1921: Duodenal ulcer following burn found at necropsy.

CASE 74.—Stewart,[36] 1923: A child, aged 5 years, died thirty-three days after extensive burns of the trunk and limbs and at necropsy a small acute ulcer was found in the pyloric region of the stomach.

CASE 75.—Stewart,[36] 1923: A man, aged 50 years, died thirteen days after very extensive burns of the trunk and limbs and at necropsy multiple acute ulcers were found in the duodenum.

CASE 76.—Ronchese,[37] 1924: F. F., a governess, aged 23 years, received third degree burns (some second degree on upper abdomen) from an alcohol lamp. Hemorrhage occurred from the bowel on the twelfth and fourteenth days, the latter being fatal. Necropsy revealed congestion of the small intestines and a recent ulcer in the descending part of the duodenum.

CASE 77.—Novak,[97] 1925: A woman, aged 20 years, with third degree burns of the legs, arms, and left breast, was treated with picric acid. During the eleven days of life, there was fever to 103° the last eight days and vomiting, diminished urine secretion, but no melena. She became comatose before death and a diagnosis of uremia was made. Necropsy revealed about forty small ulcers of the stomach, all within 3 inches of the pylorus. These penetrated to the submucosa and were surrounded by small round cells.

CASE 78.—Harris,[38] 1929: E. H., female, aged 3½ years, received second and third degree scalds of the back from the angles of the scapulae to the popliteal spaces. Tannic acid solution was applied locally and a blood transfusion given to combat surgical shock. The temperature was 102° the second day and she vomited. The third day she vomited blood and died forty-eight hours after the burn. Marked hemorrhage into the left suprarenal and a shallow duodenal ulcer 0.5 cm. below the pylorus and measuring 1 by 0.5 cm. with a blood clot in its base were found at necropsy.

CASE 79.—Levin,[60] 1929: A negro child, female, aged 4 years, had severe shock following scalds of the arms, neck, chest, abdomen, back, and left leg. The second day the temperature rose to 102° F. and varied from 99° to 102° until death on the tenth day. At necropsy the wounds were found to be septic. A perforated ulcer of the anterior surface of the first portion of the duodenum was present. There were no intestinal contents in the peritoneal cavity and death was attributed to bronchopneumonia.

CASE 80.—Levin,[60] 1929: Necropsy of a child who died of burns revealed a duodenal ulcer.

CASE 81.—Maes,[31] 1930: A white boy aged 11 years, received first degree burns of both legs and thighs. The second day the temperature was 100.8° F. and the pulse 160 and he vomited. He improved until the seventh day when hematemesis and melena occurred with anemia. The eighth day melena was marked; the blood pressure fell to 88/0; and the abdomen became tender and distended. Despite two blood transfusions, marked blood appeared in stools and death occurred on ninth day. Necropsy: Acute splenitis, acute glomerulonephritis, ileum full of blood, 8 mm. diametered ulcer in duodenum at junction of first and second portions about to perforate, larger superficial ulcer on opposing surface. Death from hemorrhage.

CASE 82.—Riehl,[39] 1930: K. M., boy, aged 6 years, received third degree burns of the extremities. On the second day his temperature went to 40° C.; the sixth day he vomited blood and on the eighth day he died. Necropsy revealed edema of the brain and clotted blood in the intestines. Two centimeters below the pylorus was a 1.3 cm. diametered ulcer, in the base of which was an open artery with a clot in the stump of it.

CASE 83.—Riehl,[39] 1930: W. N., boy, aged 18 months, received second and third degree burns of the face, arms, and chest covering 6 to 7 per cent of the body surface. Temperature rose to 40° C. after the second day. There was no emesis. Death occurred on the eleventh day. Necropsy revealed bronchopneumonia, parenchymatous degeneration of organs, clotted blood in the stomach and duodenum, and an ulcer in the posterior wall of the duodenum with the pancreas forming its base.

CASE 84.—Riehl,[39] 1930: G. E., schoolgirl, aged 7 years, received severe third degree burns on the trunk including the abdomen, arms and legs, involving 25 per cent of the body surface. She was given a blood transfusion the same day. A high fever was present after the second day. On the fourth day she vomited; the fifth day she had dark stools followed by bright fluid blood and she died the eighth day. Necropsy revealed considerable blood in the intestines and a single ulcer on the posterior wall of the duodenum adjacent to the pylorus with an eroded artery in the crater of the ulcer.

CASE 85.—Riehl,[39] 1930: F. H., a woman, aged 49 years, attempted to commit suicide by burning herself with oil. Fully one-third of the body surface, including the abdomen and genitalia, was burned. A blood transfusion was given on admission and, despite an absence of vomiting or other gastrointestinal symptoms, she died on the ninth day. Necropsy revealed two ulcers on the lesser curvature of the stomach. A cicatrization was present in the duodenum just beyond the pylorus. The gastric ulcers were definitely fresh.

CASE 86.—Riehl,[39] 1930: M. Sp., a woman, aged 49 years, received burns of about 18 per cent of the body surface on the head, upper trunk, and arms. Blood transfusion of 400 c.c. was given on day of admission. There was considerable vomiting. On the third day erysipelas developed in the incision used to expose the saphenous vein for transfusion. High temperature and death occurred on the fifth day. Necropsy revealed two fresh duodenal ulcers near the pylorus about 3 by 2 cm. There were multiple hemorrhages in the adrenals.

CASE 87.—Laird and Wilkerson,[98] 1931: A colored girl, aged 5 years, received tannic acid treatment for burns of the entire anterior portion of the body. She became suddenly worse and died seventeen days later. At necropsy a duodenal ulcer 2 cm. in diameter was found, exposing the pancreas and associated with hemorrhagic areas throughout the intestines, blood in the stomach and intestines, nephritis, and acute follicular splenitis.

CASE 88.—Wilson,[44] 1935: Patient, aged 17 months, had very deep and very extensive burn with infection by *Streptococcus hemolyticus*. The patient died on the eleventh day and at necropsy a duodenal ulcer was found.

CASE 89.—Wilson,[44] 1935: Patient, aged 16 years, had very deep and very extensive burn with infection by *Streptococcus hemolyticus*. The patient died on the twelfth day and at necropsy a duodenal ulcer was found.

CASE 90.—Willems and Kuhn,[41] 1936: Duodenal ulcer after burn verified at necropsy.

CASE 91.—Lee, W. E.,[99] 1937: Duodenal ulcer following burn.

CASE 92.—Glover,[100] 1937: Child with duodenal ulcer following burn found at necropsy.

CASE 93.—Glover,[100] 1937: Child with duodenal ulcer following burn found at necropsy.

CASE 94.—Author's case,[101] 1937: D. Mc., girl, aged 4 years, previously well, took a slide down the back of a bathtub into hot water with her clothes on. The mother applied lard and soda to the burned areas and brought her to the hospital within an hour. The child had first and second degree burns anteriorly from the level of the xiphoid process to the lower third of the thighs, over the entire buttocks and thighs, over the arms, wrists, and ankles, but not on the legs, forearms, feet, hands, shoulders, head or neck. Certain areas were third degree.

The vaseline dressings were continued. Intravenous medication was attempted but was unsuccessful, so 100 c.c. of Ringer's solution was given subcutaneously and

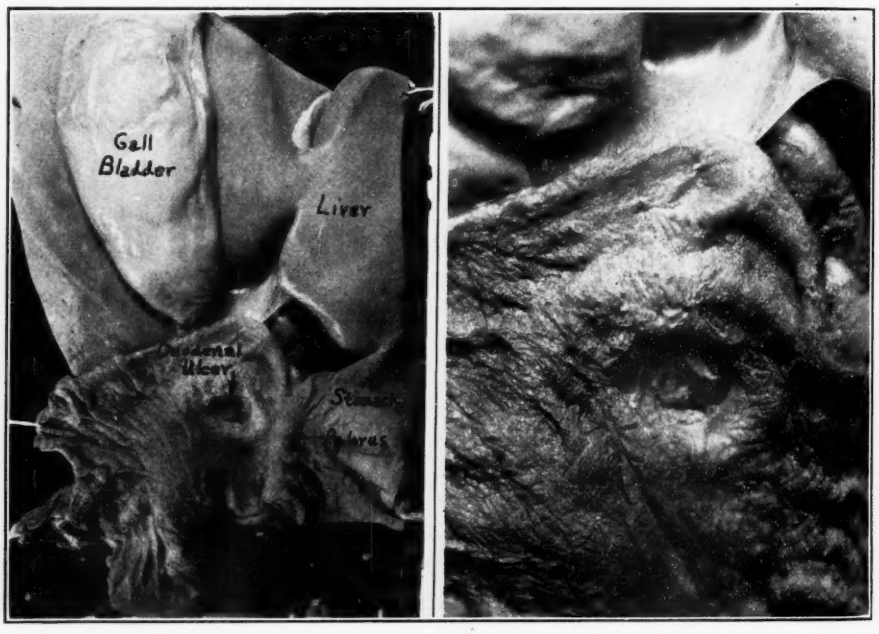


Fig. 1.—*A*, View of ulcer 2 cm. from pylorus with gall bladder and liver above, duodenum to the left and stomach to the right; *B*, closeup of the same.

fluid was begun immediately by mouth and by rectal retentions. During the next eleven days before death, fluids were forced. The patient's temperature for the first three days ranged between 38.1° and 38.8° C.; from then on it varied from 38.8° to 40.4° C. The first urinalyses and blood counts were taken three days after admission when the urine was normal; the white count, 6,600; red count, 4,500,000; and hemoglobin 95. No blood pressure reading was recorded. On the eighth day the white count had fallen to 4,500 and the red count to 3,800,000.

At this time a left peritonsillar abscess was found and 15 c.c. of thin purulent material obtained on incision which on culture showed *Streptococcus viridans* and *Staphylococcus aureus*. There was some infection of the burned areas on the buttocks. Swelling of the right forearm was noted at the same time and on the ninth day the patient became delirious. On the tenth day albumin and red cells were noted in the urine and the swelling of the right arm extended to the axilla and both legs were swollen. On the eleventh day there was gangrene of the right

hand and no pulsation was felt distal to the right axillary artery. Cyanosis was present to the elbow; râles, in the lungs; the white count was 6,300 and red count 4,300,000; and the patient died without symptoms of abdominal distress and with no vomiting after the seventh day. No stool analyses were performed but no gross blood was noted.

Necropsy was limited to the abdominal organs with visualization of the thoracic organs in situ.

Anatomic Diagnosis.—Extensive burns (first, second, and third degree) with crusted and moist denuded areas on the trunk and extremities involving about one-

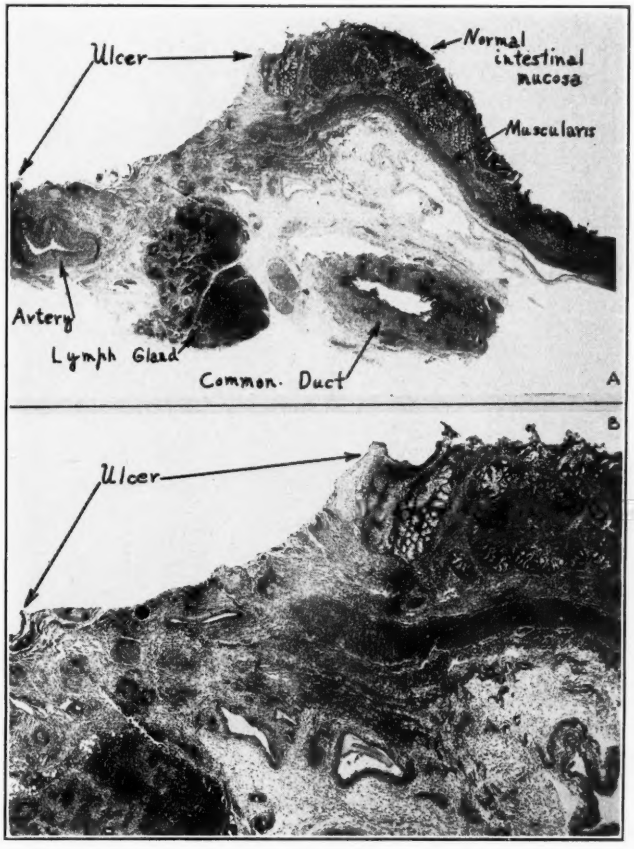


Fig. 2.—*A*, Cross-section of ulcer (×12) in Case 94. Beneath the ulcer to the left is a large vessel probably a branch of the pancreatico-duodenal artery. In the center is a lymph gland and to the right is the common duct. *B*, Higher power (×35) magnification of the same. Note the absence of cellular or proliferative action at the edge of the ulcer. Its margin is sloping and clear cut rather than rolled or curled.

fifth of the body surface. Beginning focal epidermal regeneration. Edema of the extremities, most marked in the right arm. Multiple arterial and venous thrombi in the soft tissues of the left shoulder, with beginning gangrenous necrosis. Bilateral hemorrhages in the adrenal glands. Penetrating acute duodenal ulcer (Curling's ulcer). Generalized pulmonary edema with hypostatic hyperemia. Slight left hydrothorax. Passive hyperemia of the liver and kidney with parenchymatous degeneration. Focal subacute proliferative glomerular interstitial nephritis. Focal subacute myocarditis. Left cervical lymphadenitis. Hyperplasia of the spleen.

There was no peritonitis and no hemorrhage into the intestinal tract. The stomach and pyloric ring were normal. Five centimeters below the latter in the posterior wall of the duodenum was a deep, sharply punched out ulcer measuring 1 cm. in diameter as shown in Fig. 1. The duodenal mucosa appeared to be rolled under at the ulcer margin. The ulceration had progressed entirely through the submucosa and muscular layers of the duodenum. The base appeared to be formed by a thin layer of fibrous tissue and the lateral walls of the ulcer were only slightly indurated. A small amount of pancreatic tissue separated the upper part of the ulcer from the superior wall of the portal vein upon which it rested. At the margin of the lower part of the ulcer only the reflected peritoneum separated it from the abdominal cavity. The peritoneum in this vicinity was smooth and of normal color. The duodenum was bile stained. The mucosa of the rest of the gastrointestinal tract, including that of the rectum, was normal.

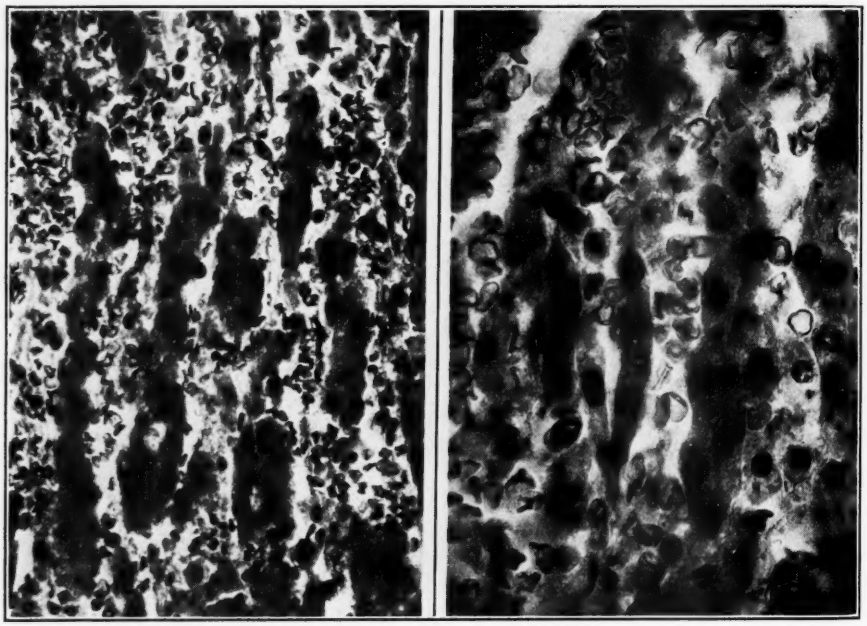


Fig. 3.—*A*, Hemorrhage in corticomedullary zone of left suprarenal gland in Case 94 (×500). Numerous erythrocytes are seen between the cords. The same microscopic picture existed in the gland on the right side only to a less extent. Little necrosis is present. *B*, Higher power (×1100) magnification of the same.

The left suprarenal was dark red in color. The surface made by cutting of the cortex was markedly thinned. Instead of being a yellowish color it was grayish red. The central portion was infiltrated with blood. In one portion in the upper pole it was almost completely destroyed by hemorrhage. The changes in the right suprarenal were similar but less marked.

Microscopic.—A section through the ulcer showed that away from the margin the duodenum was normal. The walls of the ulcer were steep, as seen in Fig. 2, and its floor lay well beneath the level of the muscularis. It had the appearance of an acute ulcer with almost no inflammatory reaction, although in the necrotic margin leucocyte outlines were seen, both mononuclear and polymorph. Two small vessels near the floor were almost occluded by intimal proliferation. A larger artery and vein a little deeper were patent. There was almost no reaction in the coats of the duodenal wall at the ulcer margin. Deeper there was a little fibrin in the

edematous retroduodenal tissues and a proliferation of fibroblastic cells about blood vessels. Sections of the suprarenals showed hemorrhages in the medulla and corticomedullary junction, especially in the reticular and fascicular zones (Fig. 3).

ANALYSIS OF 94 CASES WITH NECROPSY

On the basis of the 94 cases, an analysis is made of the type of patient attacked, the degree and type of the burn, the symptoms and the location and character of the ulcers. No especial seasonal incidence was noted. It is of interest that 2 of the patients presented a history of previous burn. Welti's patient (Case 42) was burned several months before and Hills' patient (Case 40), who was now scalded, presented scars from an extensive burn received thirteen years before.

1. *Age.*—The average age in 74 cases was 14.6 years.* The age distribution shown in Table III shows a more marked predilection for the first decade than this average would indicate, with 61 per cent of the cases occurring in this decade. It is quite possible that, as Erichsen,[15] 1844, pointed out, this is partly because children were burned more frequently. This applies especially to the era when most of these cases were reported and burns were mainly home accidents to children rather than industrial accidents to adults. The youngest patients were those of Ashby,[95] 1917 (11 weeks, Case 70); Riehl,[39] 1930 (18 months, Case 83); and Wilson,[44] 1935 (17 months, Case 88). The oldest patients were those of Hewett,[32] 1848 (66 years, Case 25); and Perry and Shaw,[12] 1894 (70 years, Case 50).

TABLE III

AGE DISTRIBUTION BY DECADES OF PATIENTS WITH GASTRIC OR DUODENAL ULCER FOLLOWING BURNS

AGE IN YEARS	0-10	11-20	21-30	31-40	41-50	51-60	61-70
Number of Cases	45	13	8	1	5	0	2

2. *Sex.*—In 65 instances the sex was stated and of these 47 were females and 18 males. The high incidence in females of 72 per cent is possibly because they were burned more frequently in the preindustrial era when most of the cases were reported. Working around kitchen stoves combined with a more inflammable costume are causes to be considered. It is quite possible, therefore, that the ulcers occurred more often in females because they were more frequently burned.

3. *Geographical Distribution.*—Most of the early ulcers were reported by authors in Great Britain, but more recently Germany and Austria and still more recently the United States have reported the majority. Of the 94 cases, Great Britain reported 52 (England, 42; Scotland, 6; and Ireland, 4); Germany and Austria, 25; the United

*This includes five cases that were designated as children and assumed to average 9 years, and one case that was termed an adult and assumed to be 25 years.

States, 8, Czechoslovakia and South Africa, 2 each; and Italy, Canada, France, Poland, and Australia, 1 each. Dupuytren reported 1 of the earliest cases, but since then there have been none from France that were found for this review.

4. *Degree and Type of the Burn.*—In 41 instances the degree of the burn is stated, 38 being third degree; 2, second degree; and 1 case (Case 81), first degree. Several of the third degree burns were of the fourth or fifth degree by the Dupuytren classification, leaving exposed muscles, fat, tracheal rings, or bones. The area of the burn was usually not computed except by Riehl who stated it was 7, 25, 33, and 18 per cent in Cases 83 to 86 respectively. In some other instances a description of the burn indicated that it involved up to even 80 per cent of the body surface. It is of interest that practically all of the patients, with the exception of Cooper's Case 7, were of sufficient magnitude to be hospitalized throughout the course of the burn. This may lead to an error in statistics since as a rule only hospitalized cases are necropsied.

In 52 cases there was sufficient data to tell whether the burn involved the abdominal wall or, in a few instances, the lower portion of the back. Such involvement was present in 23 cases and definitely stated to be absent in 29 cases (abdominal wall involvement, 44 per cent). This affords the first statistical evidence against Underhill's theory that local hyperthemia is the cause of Curling's ulcer.

In most cases the injury was a true burn and only a few cases, such as Cases 7, 18, 29, 32, 38, 40, 47, 48, 78, and 79, totaling 10 cases out of 94, were scalds.

5. *Symptoms.*—

a. *Hemorrhage:* Hemorrhage from the ulcer was noted in 27 instances and was stated to be absent in 15 instances. In 13 instances hematemesis was present and in 9 instances it was stated to be absent. Melena was present 16 times and absent 7 times. In 8 of these cases both hematemesis and melena were present. In most of these cases the hematemesis or melena was the only symptom present before death and it usually preceded death by only a day or so. Diarrhea was present several times without melena. It is interesting that of 36 cases with data adequate for analysis it was the pancreaticoduodenal artery that was eroded and which caused the hemorrhage in 13 cases. Thus in the 27 cases of recorded hemorrhage almost exactly 50 per cent were caused by erosion of this artery alone. Collin,[13] 1894, in speaking of duodenal ulcer not caused by burns, says that the pancreaticoduodenal artery was most often eroded (13 times in his series), the right gastro-epiploic artery being second (3 times). The usual case for the ulcers following burns was for the ulcer of the duodenum to erode the pancreas and for either one or two open-mouthed ends of the artery to

be seen in the depths of the ulcer. Before making the presence of melena or hematemesis after burns an operative indication, it is to be remembered, as Erichsen,[15] 1844, pointed out, that in many cases of congestion of the mucous membranes following burns there is bleeding and even at necropsy the bleeding point is not found. This might have been the case of another of the 5 patients in the author's series who died of burns. A man, aged 44 years, with very severe burns vomited so continuously that a constant suction nasal catheter was placed into the stomach. On the seventh day blood came from the catheter in small amounts and the same day the patient died with *Streptococcus hemolyticus* pyarthrosis of the left knee. No necropsy was performed.

b. *Perforation:* In 14 of 49 cases of duodenal ulcer there was perforation of the ulcer. In only 1 instance did a gastric ulcer perforate. It is interesting that of these cases in only 3 was there a definite mention of peritonitis and in 6 peritonitis was definitely stated to be absent. In several instances the opening was covered with fibrin and in 1 instance (Case 9) it was tamponaded by the gall bladder. It seems that a possible explanation for the low incidence of peritonitis may be that the edges of these ulcers have been repeatedly reported as being softer than in the usual peptic ulcer where the edges are cartilage-like. It is understandable that the walls of a soft-edged ulcer could more easily collapse together after the first perforation and prevent further escape of intestinal contents. Penetration of the ulcer to or through the muscularis or even to the serosa was noted several times. It is of interest that in 38 cases with data sufficient for analysis, penetration to and exposure of the pancreas in the base of the ulcer was noted 18 times. (This includes the series of 76 duodenal cases only.) Collin,[13] 1894, stated that in his series of ordinary peptic duodenal ulcers the pancreas played the rôle of tampon most often (27 times).

c. *Vomiting:* In 31 instances with data sufficient for analysis, vomiting occurred in 26. It is quite probable that it did not occur in many of the cases where a definite statement as to its absence was not made. As mentioned above in 13 of these 26 cases, blood was present in the vomitus.

d. *Abdominal Pain and Tenderness:* Data as to the presence of these symptoms are meagre and it is possible that they were not often present. In 7 cases abdominal pain was present (Cases 10, 12, 15, 24, 31, 32, and 59) and in 3 cases it was stated to be absent (Cases 26, 49, and 85). Abdominal tenderness was present 3 times (Cases 9, 33, and 81).

e. *Sudden Onset:* In 19 of 44 cases with data sufficient for analysis, the first symptoms of ulcer did not develop until within twenty-four hours of the time of death. In these cases the patient was progressing nicely until hematemeses, etc., supervened and within twenty-four

hours he was dead. In a few other cases, while the course was stormy, the intestinal symptoms came on only at the end.

f. *Septic Changes in the Burned Area:* In 24 instances mention was made of septic change in the burned area or of high fever, metastatic abscesses, etc. High fever; exposure of fat, muscle, tracheal rings, and bones; and secondary erysipelas, peritonsillar abscess, and panophthalmitis were mentioned. Sloughs were frequent. In only a few cases was the type of therapy originally used on the burn quoted. Flour was used 3 times, bread poultices and carron oil being mentioned. Picric acid was used in Case 77 and tannic acid in Case 87 and possibly in a few others. The small number of cases that were treated with tannic acid is of interest.

6. *Location and Character of the Ulcers.*—The most usual site of the ulcers was in the duodenum. This localization agrees with that of previous authors, including Curling's original report. Of 29 cases collected by Thiele,[14] 26 were in the duodenum and 3 in the stomach. Some authors found the stomach to be especially attacked. Novak[97] (Case 77), Dupuytren[8] (Case 2), and Leonard and Dayton[102] reported instances of multiple ulcers of the stomach following burns. In the present series, of the 94 cases, 71 were in the duodenum alone, 16 in the stomach alone, and 5 in both; 1 case was in the ileum and stomach and another in the intestine and stomach. The incidence of duodenal involvement is thus 81 per cent. This agrees with the proportion reported by some other authors for spontaneously occurring ulcers. Ulcers in other parts of the intestinal tract following burns have been reported by Hymphrey,[103] 1855 (esophagus); Fischer,[104] 1893 (esophagus); Sacconaghi[105] (ileum); and Johnson,[7] 1833 (Case 3, ileum and stomach; Case 5, intestine and stomach).

In 33 instances where the distance of the duodenal ulcer from the pylorus was stated, in 26 cases (81 per cent) the ulcer was within 1 inch of the pylorus. In 18 cases it lay over the pancreas which was eroded.

The incidence of perforation, hemorrhage, exposure of pancreas, and erosion of arteries has already been discussed. In several instances the ulcer was said to be healing at the time of necropsy and in others it was said to be definitely acute, as in Cases 53, 75, and 85.

When the duodenum alone was involved, the ulcers were multiple in 23 cases and single in 47 cases. When the stomach alone was involved, the ulcers were multiple in 6 cases and single in 10 cases. When both organs were involved, the duodenal ulcers were multiple 2 times and single 3 times and the stomach ulcers were multiple 4 times and single once.

7. *Age of the Ulcers.*—It is, of course, of vital importance to be sure in each case that the ulcer did not antedate the burn. Fraenkel,[25] 1898, saw an ulcer following death from a burn in the stomach of a girl,

aged 5 years, that he believes antedated the burn. This author reported no true Curling's ulcer in 34 consecutive burn necropsies in nine years. Kuttner,[106] 1908, cited a boy who died of pulmonary embolism seventeen days after a burn with the pathologic finding of an ulcer and stated: "The ulcer is without doubt much older than 17 days." Hansemann,[107] reported an ulcer in a patient dying two days after a burn, but believed the ulcer was at least a month old. Schmorl[108] also reported an ulcer that he believed to be older than the burn. Perry and Shaw,[12] 1894, in speaking of one of their cases (Case 43), state that to the eye the ulcer had thickening around the edge to an extent that would tend to make one believe it older than the burn, but when one felt it there was not the induration such as one would expect to find in a chronic ulcer. This lack of induration is mentioned by several other writers.

In the present series, in 68 cases with data adequate for analysis, the average time that elapsed from the burn until death was 15.4 days. It is quite probable that the length of life of the patient was greater than the duration of the ulcer. Furthermore, in several instances death was definitely not due to the ulcer, in Cases 8 (death at 28 days), 19 (30 days), and 34 (42 days) it was said to show signs of healing. Counting only the 31 cases where the ulcer was associated with definite perforation or hemorrhage, death occurred an average of 12.8 days after the burn. This figure probably represents a truer figure for the time after a burn when one should expect death from an ulcer to be most likely to occur. The minimum time interval reported was 18 hours by Ponfick,[62] (Case 38), other low figures being 36 hours by Dupuytren[8] (Case 2), 48 hours by Swan[5] (Case 1) and Harris[38] (Case 78), and 83 hours by Hills[59] (Case 40). None of these cases showed perforation and only Harris' bled so it is quite possible that death was from the burn itself and the ulcer had only begun to form. The longest time interval reported between the burn and death was 75 days by Hewett[32] (Case 27). Another factor to be considered in calculating the age of the ulcer is that in many of the 13 cases where the ulcer had eroded the pancreaticoduodenal artery the ulcer showed signs of healing. Without the accident of the erosion, the patient might have gone on to recovery. Thus, Luke,[82] 1844, in speaking of Case 24, says that the ulcer showed signs of healing and might have continued to do so if the hemorrhage had not occurred.

DOUBTFUL CASES

In this review of the literature several references to cases were found in the article of Hofmann[109] cited by Schjerning,[11] 1884, or in the articles of Faber[110] or Nauwerck[111] cited by Riehl,[39] 1930. Riehl quoted Sternberg as having seen two cases yet this author himself[112] said he had seen none. Riehl also stated that Weidenfeld and Zumbusch,[93] 1905,

never saw a case, yet these authors report one which is included in the present series. The reference for the case of Demme of an ulcer found seven and one-half hours after a burn also cited by Riehl could not be found. Pitt's,[113] 1886, case of superficial erosions of the stomach found in a man, aged 64 years, dying four days following a burn, is not included. The case of Leonard and Dayton,[102] 1917, of a woman, aged 52 years, who died the fourth day after receiving the Percy "cold iron" treatment for carcinoma of the cervix is not included in the present report. At necropsy death was found to be due to pulmonary embolism and there were twenty-four round ulcers 1 to 7 mm. in diameter in the stomach extending down to the muscularis, and infection was marked in the uterus. The authors stated, "a mass of sloughing coagulated tissue of this type offers an ideal medium for the growth of microorganisms . . . once infected the thrombosed vessels of the region may offer a ready entrance into the system," and consider septicemia a possible cause of the ulcers.

CONGESTION OF THE STOMACH AND DUODENUM

This finding has been noted by many authors following burns besides the reports of Cumin,[6] Dupuytren,[8] Long,[3] Curling,[1] and Hewett[32] already mentioned. Bardeleben,[114] 1852; Klebs,[115] 1884; Welti,[116] 1890; Bowlby,[117] 1890; Swain,[118] 1893; Dohrn,[22] 1901; Kirchmayr,[119] 1922; Levin,[60] 1929; and D'Ewart,[120] 1930, all reported cases. In 63 burn necropsies, Schjerning,[11] 1884, noted hyperemia of the stomach 10 times, hyperemia of the intestines 20 times, and ecchymoses of the intestines twice. Perry and Shaw,[12] 1894, collected reports of 5 cases of duodenal congestion following burns. Marchand,[26] 1908, noted the condition a few times in a series of 50 burn necropsies. It is quite possible that some of these cases might have gone on to ulceration, especially since some of them, such as the case of Welti, died very soon, sixty hours in this instance, after the burn. This was not invariable and some of these cases died over two weeks after receiving the burn.

ULCER OF THE GASTROINTESTINAL TRACT FOLLOWING BURNS WITH RECOVERY

In several instances when death followed some other cause, the patient with ulcer might have gone on to recovery. This applies, for example, to Case 19 where death from pneumonia occurred thirty days following the burn and Case 43 which died of tetanus 13 days following the burn. Cases 8 and 34 are also examples of ulcers that might have gone on to recovery. Eichhorst,[121] 1888, reported the necropsy of a man, aged 46 years, who died twenty-three years after an extensive burn of the right thigh with carcinomatous degeneration of an ulcer 2 cm. below the pylorus. The relationship between the burn and

the subsequent necropsy finding is difficult to prove. The oft-quoted case of Simpson,[122] 1889, is even less likely to be an ulcer due to burns. The diagnosis of the ulcer was based on the presence of fever, constipation, and pain and tenderness in the abdomen.

Thirteen cases of probable ulcer of the gastrointestinal tract have been reported, however, as follows:

REPORT OF CASES WITH RECOVERY

CASE 95.—Hertz and Digby,[76] 1913: E. J., a female cook, aged 35 years, had hematemesis twenty-seven days after a third degree scald of the left foot. Hematemesis continued for several days; the red count was 2,200,000 and the hemoglobin 25 per cent; and there was melena until the forty-third day. Two and one-half months later the red count was 4,000,000 and the patient recovered.

CASE 96.—Kirchmayr,[119] 1922: K. J., male, aged 22 years, had a third degree burn of neck, back, and right arm in 1907 for which he was hospitalized fifteen days. He had abdominal pain thereafter which interfered with his schoolwork in 1908. The pains continued one to two hours after meals until a hematemesis in 1917. In 1919 an x-ray showed pyloric obstruction and a gastric resection was done for duodenal ulcer.

CASE 97.—Maes,[31] 1930: A man, aged 48 years, had symptoms of duodenal ulcer following a burn of the chest, epigastrium, and legs. Twenty years later an operation for inoperable carcinoma of the upper abdomen was done.

CASE 98.—Clements,[123] 1932: A man who was scalded over the entire body below the shoulders developed ulcer symptoms eleven weeks later which improved on ulcer diet and treatment.

CASE 99.—Fitzgibbon,[124] 1932: A man, aged 37 years, had abdominal pain two weeks and acute melena five weeks after a burn. Roentgen examination confirmed the presence of duodenal ulcer and the patient recovered. (N.B. This patient complained of some abdominal distress a few months before the accident, but Roentgen examination at that time of the stomach and duodenum were entirely negative.)

CASE 100.—Fitzgibbon,[124] 1932: An ulcer was diagnosed six months after a burn in a man, aged 61 years, and was confirmed by Roentgen examination.

CASE 101.—Miller and Rubenstein,[125] 1932: A man was burned and treated with butyn and picric acid. After a septic course with fever to 103° F., melena and hematemesis suddenly began on the eleventh day. This was so severe that the red count was 2,500,000; hemoglobin was 55 per cent; and the patient was given three blood transfusions. An x-ray six weeks later was suggestive of duodenal ulcer and the patient went on to recovery.

CASE 102.—Torchiana,[126] 1936: A male laborer, aged 55 years, had abdominal pain several weeks after a burn of the thorax and Roentgen examination revealed a duodenal ulcer. This ulcer perforated after eight months and following a gastroenterostomy and closure of the opening the patient recovered.

CASE 103.—Sherrill,[127] 1937: A boy, aged 6 years, with extensive third degree burns of the trunk and extremities was treated with tannic acid. He was well until the seventh day when abdominal pain began. The next day melena began. This was so severe that a transfusion was given the ninth day. By the fourteenth day the pain and melena finally ceased and the patient recovered.

CASES 104-107.—Glover,[100] 1937: Four patients developed an ulcer of the duodenum following burns. Three were diagnosed by x-ray and the fourth required later gastric resection.

The presence of ulcer in all of these cases is not certain. In 8 instances there was Roentgen confirmation of the diagnosis. In 4 cases operation was performed. Epigastric pain was stated to be present 5 times; melena, 4 times; hematemesis, 3 times; and marked anemia, twice. In 2 instances blood transfusions were given. With such a small series of cases, the incomplete analysis of signs and symptoms in some of them, and in certain instances the long time interval between the burn and subsequent development of symptoms and signs of the ulcer, the possibility that the ulcers were only coincidental cannot be ruled out.

DUODENAL ULCERATION FOLLOWING FREEZING

Foerster,[128] 1861, reported the case of a man, aged 20 years, who fell asleep in the snow while drunk and froze both feet and died a few days later with signs of intestinal perforation. Necropsy revealed that the legs were gangrenous and the thighs edematous. There were five or six small fresh ulcers of the duodenum, one of which had perforated with resultant peritonitis. There was no induration of the wall of the ulcers. The author was uncertain as to whether the ulcers were due to the freezing or to the liquor the patient had taken. Adams,[129] 1863, reported the case of Private C., aged 36 years, whose feet were frozen to the ankles with gangrene during the Civil War. Seven days later diarrhea and emaciation set in and he died the twenty-second day. Necropsy revealed numerous small, irregular, elliptical ulcers of the mucous membrane of the duodenum. In speaking of these cases, Billroth,[68] 1867, stated: "Both cases were caused according to my viewpoint by septicemia and ought not to be attributed directly to the freezing as such."

EXPERIMENTAL

The experimental work done to elucidate the problem of Curling's ulcer includes reference to the whole mass of work done on the ulcer problem as a whole. The work of Hunter,[19] 1890, and Mc Laughlin,[67] 1933, has already been mentioned. Parascandolo,[130] 1905; Vassale and Secchi;[131] and Busse,[94] 1914, injected burn extracts into experimental animals and found evidences of congestion in the stomach and duodenum. Mendel,[50] 1870; Andakow,[132] 1876; and Pfeiffer,[133] 1905, produced ulcers in experimental animals by burning. The observation of Frohner,[134] of three accidentally burned horses who died with the findings of hemorrhage of the mucous membrane of the stomach and intestines with secondary necrosis is of interest in this connection. Billroth,[68] 1867, reported that sepsis in dogs produced congestion of the duodenum.

Experiments.—A series of 19 dogs were thoroughly anesthetized with sodium barbital and then burned. In all cases the dogs died or were killed within twenty-four hours. In only 1 instance was marked congestion of the intestinal tract noted at necropsy and then it was not especially localized in the duodenum. In no case were ulcers present. No congestion of the stomach was noted. In all instances the burns were quite severe and there was marked blood pressure fall and blood concentration in most instances.

These experiments were performed before the literature on Curling's ulcer was reviewed and it is quite possible that if the animals had been observed at an interval of two weeks after the burn, more marked changes would have been observed in the intestinal tract. In these experiments no animal survived long enough for infection to develop. Even if burned dogs are allowed to live for several days, no infection develops until secondary necrosis takes place because the burned skin of dogs does not weep as in human beings. In 6 dogs where the suprarenals were examined postmortem, they were hemorrhagic in 4 animals (bilateral in 3). In none of these 4 animals were there intestinal hemorrhages or ulcers.

SUMMARY

The occurrence of gastrointestinal ulceration following burns is more common than coincidence would allow. A severe third degree burn, often of a sloughing septic type, is most apt to result in such an ulceration. A decreased incidence of this complication may come from a more aseptic handling of burns. The only other therapeutic considerations are the realization of the possibility of these ulcers and institution of the proper medical or surgical treatment of them as is indicated. Up to the present time, no acute ulcer following burns has been treated surgically.

Children and females are more often affected, but this may be because they are more frequently burned. The symptoms of such an ulcer may be of rapid onset and include epigastric pain, melena, and hematemesis. The average length of life in 94 cases with necropsy collected from the literature was 15.4 days.

The ulcer involved the duodenum alone in 71 cases, the stomach alone in 16 cases, and both organs in 5 cases. The ulcer was single 57 times and multiple 34 times. Hemorrhage was twice as apt to be a fatal factor as perforation and the pancreas was often exposed and the pancreaticoduodenal artery eroded.

Thirteen reports of gastrointestinal ulceration with recovery and 2 reports of such ulceration following freezing are mentioned. Congestion of the duodenum was frequently reported.

REFERENCES

1. Curling, T. B.: On Acute Ulceration of the Duodenum in Cases of Burn, Medico-Chir. Trans. Lond. **25**: 260-281, 1842.
2. Moynihan, B. G. A.: Duodenal Ulcer, Philadelphia, 1912, W. B. Saunders Company, chap. 2, pp. 24-43.
3. Long, James: On the Post-Mortem Appearance Found After Burns, Lond. Med. Gaz. **25**: 743-750, 1840.
4. Cooper, Samuel: Pathology of Burns and Scalds, Lond. Med. Gaz. **23**: 837-838, 1839.
5. Swan, Joseph: Case of Severe Burn, Edinb. M. & S. J. **19**: 344-345, 1823.
6. Cumin, William: Cases of Severe Burn, with Dissections and Remarks, Edinb. M. & S. J. **19**: 337-344, 1823.
7. Mac Farlane, John: On Burns and Scalds, Johnson's Medico-Chirurgical Review **19**: 529-538, 1833, article written by Johnson, quoting Mac Farlane in third person).
8. Dupuytren, Baron: Clinical Lectures on Surgery (Trans. of Leçons Orales de Clinique Chirurgicale, 1832, by A. S. Doane), New York, 1833, Collins and Hannay, Publishers, p. 229-280.
9. Pack, G. T.: The Pathology of Burns, Arch. Path. **1**: 767-805, 1926.
10. Holmes, T., and Hulke, J. W.: A System of Surgery, London, 1883, Longmans, Green, and Co., Ed. 3, Vol. I, pp. 387-400, Burns and Scalds, by Timothy Holmes.
11. Schjerning: Ueber den Tod in Folge von Verbrennung und Verbrühung vom gerichtsärztlichen Standpunkte, Vierteljahrschrift f. gericht Med. N. F. **41**: 24-66, 273-300, 1884.
12. Perry, E. C., and Shaw, L. E.: On Diseases of the Duodenum, Guy's Hosp. Rep. **50**: 171-308, 1894.
13. Collin, H.: Étude sur l'Ulcère simple du Duodenum, Thèse, Paris, 1894, G. Steinheil, editeur, pp. 1-122.
14. Thiele, P.: Beitrag zur Kenntnis der Geschwürsbildungen des Magen und Duodenum im Kindesalter, Deutsche Ztschr. f. Chir. **150**: 275-286, 1919; Thiele, P.: Über geschwürsbildungen des Gastro-Duodenaltractus in Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **16**: 302-383, 1919.
15. Erichsen, J. E.: On the Pathology of Burns, Lond. Med. Gaz. **31**: 544-553, 1843.
16. Kaufmann, E.: Pathology, Vol. III, pp. 2082-2083; American translation by Reimann, S. P., Philadelphia, 1929, P. Blakiston's Son & Co.
17. Fenwick, S., and Fenwick, W. S.: Ulcer of the Stomach and Duodenum, Philadelphia, 1900, P. Blakiston's Son & Co., pp. 87, 109-112.
18. Wilks, S.: Report of the Post-Mortem Examinations of the Cases of Burn Occurring During the Last One and a Half Year [sic], with Reference to the Condition of the Duodenum, Guy's Hosp. Rep. **17**: 133-136, 1856.
19. Hunter, William: The Pathology of Duodenitis after Burns, Brit. M. J. **1**: 76-77, 1890.
20. Fayrer: Cited by Hunter.[19]
21. Falk, Friedrich: Ueber einige Allgemeinerscheinungen nach umfangreichen Hautverbrennungen, Virchow's Arch. f. Path. Anat. **53**: 27-69, 1871.
22. Dohrn, K.: Zur pathologischen Anatomie des Frühtodes nach Hautverbrennungen, Deutsche Ztschr. f. Chir. **60**: 469-499, 1901.
23. Reuter, Versé, Dietrich, Fahr, and Chiari: Cited by Busse,[94]
24. Bardeen, C. R.: A Study of the Visceral Changes in Extensive Superficial Burns, J. Exper. Med. **2**: 501-514, 1897; Bardeen, C. R.: A Review of the Pathology of Superficial Burns, With a Contribution to Our Knowledge of the Pathological Changes in the Organs in Cases of Rapidly Fatal Burns, Johns Hopkins Hosp. Rep. **7**: 137-179, 1898.
25. Fraenkel: 1898, in discussion of article by Simmonds.[34]
26. Marchand, F., in Krehl, L., and Marchand, F.: Handbuch der Allgemeinen Pathologie **1**: 80, 1908; S. Hirzel, Leipzig; Marchand, F.: Ueber Ulcus Duodeni, München. med. Wchnschr. **60**: 1410, 1913.
27. Brunner, F.: Das acut in die freie Bauchhöhle perforirende Magen- und Duodenalgeschwür, Deutsche Ztschr. f. Chir. **69**: 101-235, 1903.
28. Fenwick, W. S.: Ulcer of the Stomach in Children, Internat. Clin. (7th Ser.) **2**: 165-177, 1897.
29. Cutler, E. G.: Gastric Ulcer in Children, Boston M. & S. J. **151**: 367-372, 1904.

30. Ewald, C. A.: Ueber Duodenalgeschwüre, Deutsche med. Wchnschr. **38**: 785-787, 1912.
31. Maes, U.: Curling's Ulcer: Duodenal Ulcer Following Superficial Burns, Ann. Surg. **91**: 527-532, 1930; Maes, U.: A Consideration of Curling's Ulcer, with Report of Two Cases, M. Rec. **24**: 564-568, 1930.
32. Hewett, P.: Ulceration of the Duodenum in Cases of Burns, Illustrated by a Specimen, Tr. Path. Soc. Lond. **1**: 256-259, 1846-1848.
33. Erichsen, J. E.: The Science and Art of Surgery, Ed. 10, **1**: 395-396, London, 1895, Longmans, Green, and Co.
34. Simmonds: Ueber Duodenalgeschwüre bei Kindern, München. med. Wchnschr. **45**: 434-435, 1898.
35. Gruber, G. R.: Zur Lehre über das peptische Duodenalgeschwür, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **25**: 465-526, 1913.
36. Stewart, M. J.: The Pathology of Gastric Ulcer, Brit. M. J. **2**: 955-957, 1021-1025, 1923.
37. Ronchese, Francesco: Ulcera Duodenale in un Caso di Gravi Scottature, Riforma med. **40**: 753-755, 1924.
38. Harris, R. I.: Fatal Burn: Death Due to Haemorrhage Into the Suprarenal Capsule and to Haemorrhage From a Duodenal Ulcer, Brit. J. Surg. **16**: 677-680, 1929.
39. Riehl, G., Jr.: Über Ulcus pepticum bei Verbrennungen, Acta dermat.-venereol. **11**: 277-294, 1930.
40. Brinkman, F.: Beitrag zur Statistik des runden Magengeschwürs, Inaug. Dissert., Kiel, 1915, 1-23.
41. Willems, J. D., and Kuhn, L. P.: Burns, A Statistical Study of 1206 Cases, Am. J. Surg. **34**: 254-258, 1936.
42. Fourcault, Gluge, Gerlach, Ducros, Magendie, Becquerel, Breschet, and Balbiani: Cited by Brown-Sequard.[47]
43. Cooke: Cited by Pack.[9]
44. Wilson, W. C.: Extensive Burns and Scalds, Edinburgh M. J. **52**: 177-188, 1935.
45. Underhill, Frank P., Kapsinow, Robert, and Fisk, Merl E.: Studies on the Mechanism of Water Exchange in the Animal Organism, I. The Nature and Effects of Superficial Burns, Am. J. Physiol. **95**: 302-314, 1930.
46. Gibbon, S.: Ulcerated Duodenum, Taken from a Man Who Died in Consequence of an Extensive Scald, Tr. Path. Soc. Lond. **6**: 189-190, 1854-1855.
47. Brown-Séquard, E.: Course of Lectures, Lancet **2**: 545-547, 1858.
48. Leube: Cited by Pack.[9]
49. Catiano: Über die Störungen nach ausgedehnten Hautverbrennungen, Virchows Arch. f. path. Anat. **87**: 345-363, 1882.
50. Mendel, E.: Ueber die Ursachen des Todes nach ausgedehnten. Verbrennungen der Haut, Vierteljahrsschrift f. gericht. Med. **13**: 93-139, 1870.
51. Sherren, J.: The Stomach and Duodenum, in Choyce, C. C.: System of Surgery, New York, 1923, **2**: 373-374, Paul B. Hoeber, Inc.
52. Wells, H. G.: Chemical Pathology, Philadelphia, 1925, W. B. Saunders Company, Ed. 5, p. 652.
53. Pack, G. T., and Davis, A. H.: Burns, Philadelphia, 1930, J. B. Lippincott Company.
54. Kapsinow, R.: The Mechanism of Production of Curling's Ulcer, South. M. J. **27**: 500-503, 1934.
55. Blalock, Alfred: Experimental Shock. VII. The Importance of the Local Loss of Fluid in the Production of the Low Blood Pressure After Burns, Arch. Surg. **22**: 610-616, 1931.
56. Harkins, H. N.: Bleeding Volume in Experimental Burns, Proc. Soc. Exper. Biol. & Med. **32**: 3-4, 1934; Harkins, H. N.: The Bleeding Volume in Severe Burns, Ann. Surg. **102**: 444-454, 1935.
57. Brooks, B., and Blalock, A.: Shock with Particular Reference to that Due to Haemorrhage and Trauma to Muscles, Ann. Surg. **100**: 728-733, 1934.
58. Paget, S.: Duodenal Ulcer After a Burn, Brit. M. J. **1**: 128, 1890.
59. Hills, W. C.: Accidental Scald, Followed by Death on the Fourth Day. Ulcer of the Duodenum, J. Ment. Sc. **26**: 556-559, 1881.
60. Levin, J. J.: Duodenal Ulcers Following Burns: With the Report of Two Cases, Brit. J. Surg. **17**: 110-113, 1929.
61. Kraus, Klebs, and Jez: Cited by Ronchese.[37]
62. Ponfick: Ueber den Tod nach ausgedehnten schweren Verbrennungen, Berl. klin. Wchnschr. **13**: 225-233, 1876.
63. Sonnenburg, Leotta, and Ewald: Cited by Ronchese.[37]

64. Salvioli: Cited by Ronchese.[37]
65. Merkel: Cited by Busse.[94]
66. Cassanello: Cited by Ronchese.[37]
67. Mc Laughlin, C. W.: The Curling Ulcer, Study of Intestinal Ulceration Associated with Suprarenal Damage, Arch. Surg. **27**: 490-505, 1933.
68. Billroth, T.: Ueber Duodenalgeschwüre bei Septicämie, Wien. med. Wchnschr. **17**: 705-709, 1867.
69. Broadbent, J. F. H.: The Diagnosis of Perforating and of Chronic Duodenal Ulcer, Lancet **1**: 1404-1407, 1908.
70. Stengel, A.: Diseases of the Intestines, Chapter XI, Vol. III, pp. 558-559, Osler's Modern Medicine, Philadelphia and New York, 1926, Lea and Febiger.
71. Aldrich, R. H.: The Rôle of Infection in Burns. The Theory and Treatment with Special Reference to Gentian Violet, New England J. Med. **208**: 299-309, 1933.
72. Harkins, H. N.: Recent Advances in the Study of Burns, SURGERY **3**: 430, 1938.
73. Greenwood, J. R.: A Case of Fatal Ulceration of the Duodenum, Produced Through Scalding by Hot Water Used as a Haemostatic, Lancet **2**: 298-299, 1880.
74. Stallard and Borman: Cited by Pack and Davis.[53]
75. Melchior, E.: Das Ulcus Duodeni, Ergebn. d. Chir. u. Orthop. **2**: 210-277, 1911.
76. Hertz, A. F., and Digby, W. E.: Case of Recovery From a Duodenal Ulcer Produced by a Burn, Guy's Hosp. Rep. **52**: 157-160, 1913.
77. Singer, Gustav: Zur Pathogenese und Klinik des Duodenalgeschwürs, Wien. klin. Wchnschr. **34**: 43-44, 1921.
78. Rosenbach, O.: Zur Pathologie des Ulcus duodeni, Arch. f. Verdauungskr. **18**: 48-60, 1912.
79. Held: Cited by Ronchese.[37]
80. Stanley and Lee: Cited by Curling.[1]
81. Jaksch: Beitrag zur Lehre vom perforirenden Magengeschwüre, Vierteljahrschrift f. d. prakt. Heilkunde, Prague **3**: 1-17, 1844.
82. Luke: London Hospital Reports: Ulcer in the Duodenum Consequent on a Burn, Lancet **1**: 387-388, 1844.
83. Hawkins, Caesar H.: Ulcer of the Duodenum After a Burn, Tr. Path. Soc. Lond. **2**: 290-292, 1850.
84. O'Sullivan, S.: Case of Double Perforation of the Duodenum from Extensive Burns, Dublin J. M. Sc. **37**: 221, 1864.
85. Curling, T. B.: Acute Perforating Ulcer of the Duodenum, After a Severe Burn, Lancet **1**: 484, 1866.
86. Clark, A.: Cases of Duodenal Perforation, Brit. M. J. **1**: 731-732, 1867.
87. Cuthbertson, D.: Case of Ulceration of the Duodenum After a Burn, Med. Times & Gaz. **2**: 347, 1867.
88. Mc Carthy: 1874, cited by Perry and Shaw.[12]
89. Stokes: Gastric Ulcers and Perforating Ulcer of Duodenum After a Burn, Dublin J. M. Sc. **62**: 327-328, 1876.
90. Smith: Cited by Stokes.[89]
91. Halla: Cited by Schjerning.[11]
92. Welti, E.: Ueber die Todesursachen anch Hautverbrennungen, Beitr. z. path. Anat. **4**: 521-557, 1889.
93. Weidenfeld, St., and Zumbusch, L.: Weitere Beiträge zur Pathologie und Therapie schwerer Verbrennungen, Arch. f. Dermat. u. Syph. **76**: 163-184, 1905.
94. Busse, O.: Über Darmveränderungen nach Verbrennung, Verhandl. d. Deutsch. path. Gesellsch. **17**: 290-294, 1914.
95. Ashby, I. E.: Duodenal Ulcer Complicating Burns in an Infant, M. J. Australia **1**: 183, 1917.
96. Mayer: Cited by Thiele.[14]
97. Novak, E.: Gastrointestinal Ulceration Following Cutaneous Burns. With Report of Case, Am. J. M. Sc. **169**: 119-125, 1925.
98. Laird, W. R., and Wilkerson, W. V.: "Curling's Ulcer" (With Report of a Case), West Virginia M. J. **27**: 128-130, 1931.
99. Lee, W. E.: Cited by Bancroft, F. W.: Cutaneous Burns, Nelson New Loose-Leaf Surgery, New York, 1937, Thomas Nelson & Sons, Vol. 1, pp. 787-826.

100. Glover, D. M.: An Evaluation of the Tannic Acid Treatment of Burns: A Clinical Study of 556 Burns So Treated Over a Period of Eleven Years, Ohio State M. J. **33**: 146-151, 1937.
101. Case previously referred to by Harkins, H. N.: Correlation of Clinical Treatment of Burns With Recent Experimental Studies, Illinois M. J. **70**: 332-338, 1936.
102. Leonard, V. N., and Dayton, A. B.: Fatal Complications of Percy's "Cold Iron" Method in the Treatment of Inoperable Carcinoma of the Cervix, Surg., Gynec. & Obst. **24**: 156-161, 1917.
103. Humphrey, G. M.: Quoted by Hurst, A. F., and Stewart M. J.: Gastric and Duodenal Ulcer, Oxford, 1929, Oxford University Press, pp. 29, 89, 143-144, 497.
104. Fischer: Cited by Hurst and Stewart.[103]
105. Sacconaghi: Cited by Parascandolo.[130]
106. Kuttner, L.: Über das Vorkommen von Ulcus duodeni im ersten Dezennium, Berl. klin. Wchnschr. **45**: 2009-2012, 1908.
107. Hansemann: Cited by Busse.[94]
108. Schmorl: Cited by Busse.[94]
109. Hofmann, E.: Weitere Beobachtungen an verkohlten Leichen, Wien. med. Wchnschr. **26**: 145-147, 173-176, 1876.
110. Faber (Fahr): Cited by Riehl.[39]
111. Nauwerck, C.: Gastritis ulcerosa chronica. Ein Beitraz zur Kenntniss des Magengeschwürs, München. med. Wchnschr. **44**: 955-958, 987-990, 1897.
112. Sternberg: Cited by Busse.[94]
113. Pitt, G. N.: Stomach With Numerous Superficial Erosions Following After an Extensive Burn, Tr. Path. Soc. Lond. **38**: 140-141, 1886-1887.
114. Bardeleben: Cited by Mendel.[50]
115. Klebs: Cited by Marchand, 1908.[26]
116. Welti, Emil: Drei Fälle von Verbrennungstod, Centralbl. f. allg. Path. u. path. Anat. **1**: 537-550, 1890.
117. Bowlby: Cited by Hunter.[19]
118. Swain: Extensive Burn; Haematemesis; Death; Necropsy, Lancet **2**: 1127, 1893.
119. Kirchmayr, Ludwig: Ein chronisches Duodenalgeschwür nach Verbrennung, Deutsche Ztschr. f. Chir. **171**: 109-116, 1922.
120. D'Ewart, J.: Gastrostaxis Following Burns, Brit. M. J. **1**: 242, 1930.
121. Eichhorst, H.: Verbreitungsweise der Hautnerven beim Menschen, Ztschr. f. klin. Med. **14**: 519-542, 1888.
122. Simpson, J. C.: Case of Extensive Burn of Thighs and Abdomen. Probable Ulceration of Intestine. Recovery, Brit. M. J. **2**: 875-877, 1889.
123. Clements, H. J.: Are We Up to Date in Our Treatment of Burns, Northwest Med. **31**: 209-215, 1932.
124. Fitzgibbon, J. H.: Duodenal Ulcer Following Skin Burns: Report of Two Cases with Recovery, Northwest Med. **31**: 427-430, 1932.
125. Miller, T., and Rubenstein, B.: An Unusual Burn Case, Texas State J. Med. **27**: 873, 1932; Miller, T., and Rubenstein, B.: Curling Ulcer, Dallas M. J. **18**: 8-9, 1932.
126. Torchiana, Liuga: Ulcera duodenale al seguito di ustioni e sua importanza medico-legale, Policlinico (sez. prat.) **43**: 2105-2112, 1936.
127. Sherrill, W. P.: Burns, Two Case Reports of Extensive Burns in Children; Both Recovered; One with Curling Ulcer, Southwestern Med. **21**: 135-138, 1937.
128. Foerster, A.: Ulcus duodeni perforans, Würburger. med. Zeit. **2**: 164-165, 1861.
129. Adams, S.: Ulceration of the Duodenum in Severe Cases of Frost-Bite, Am. M. Times **6**: 101, 1863.
130. Parascandolo, K.: Experimentelle Untersuchungen über Verbrennung, Wien. med. Wchnschr. **54**: 575-579, 626-630, 676-680, 1904.
131. Vassale and Secchi: Cited by Hurst and Stewart.[105]
132. Andakow: Cited by Ronchese.[37]
133. Pfeiffer, H.: Experimentelle Beiträge zur Ätiologie des primären Verbrennungstodes, Virch. Arch. f. path. Anat. **180**: 367-435, 1905.
134. Frohner: Cited by Riehl.[39]

Book Reviews

Diagnostisch—Therapeutische Technik fur den Chirurgen. By Rudolph Geissendorfer. Unbound. Pp. 509, with 148 illustrations. Leipzig, 1937, Johann Ambrosius Barth, Publisher. 16.00 RM.

This volume written by the first surgical assistant of the Breslau surgical clinic is intended primarily for junior surgical house officers—for whom it will prove undoubtedly a very valuable guide in pre- and postoperative treatment. The general practitioner also will find it a good source of reference for diverse matters relating to postoperative management. In addition it contains useful chapters on wound management and the sterilization of instruments and tables which indicate the physiologic dose of drugs commonly employed by surgeons. There are sections dealing with the technique of counting blood cells and the methods of chemical analysis. To one unacquainted with the German plan of acquiring training in a clinic, these latter chapters may seem out of place. When one recalls that all diagnostic measures, including laboratory procedures, are done by the surgical assistants in the clinic, this invasion of what we would consider another pedagogic province can be understood.

The author has set himself the task of supplying junior house officers with a useful handbook which will supply their every need. He has succeeded admirably in bringing together in a small compact volume a great deal of information on a large variety of subjects which will prove very helpful to the young surgical aspirant.

Atlas of Skeletal Maturation. By T. Wingate Todd. Pp. 203, with 75 illustrations. St. Louis, 1937, C. V. Mosby Co. $7.50.

To establish standards of skeletal maturation for the osseous system is an undertaking requiring almost Herculean effort to overcome the many obstacles which beset such an investigation. To obtain standards which would be irrefutable, it was necessary first to select a group of patients whose ages ranged from infancy to the adult life. The ages from three months to sixteen years were adopted. It was necessary to keep this group of individuals as far as possible under constant surveillance. The investigation also involved the study of variances in different races, as well as the variances in environment, mental development, parentage, economic standing, stature, weight, and health of the entire group, which number 4,000. This was done to eliminate as far as possible the percentages of error.

To review over one-fourth million roentgenograms was in itself a tremendous task and could have been accomplished only by a tenacity of purpose and an indefatigable industry, all of which was portrayed by the author and his coworkers. As stated by the author, it was necessary to review, assess, segregate, and review over and over again, as well as assess and reassess, before the final standard of maturation was accepted for publication. The author was the final judge and it was therefore necessary for him to review over one-half million films.

The atlas gives only the standard of skeletal maturation for the hand of both sexes. The ages of both sexes included infants of three months of age to individuals of sixteen years. The limit of sixteen years was adopted as demonstrative of maturation in the adult.

The atlas is well illustrated with seventy-five roentgenograms of the skeletal structure of the hand. They are clear, easily interpreted, and are reproduced flawlessly. The first two chapters of the atlas are descriptive of the technical terms used and the explanation of the many trying difficulties that were overcome. The remainder of the atlas contains the flawless reproductions of the roentgenograms, first of the hand of the male and second of the hand of the female. On the page opposite each roentgenogram there is a description of the maturation of the skeletal structures of the wrist and hand.

The paper is of excellent texture and the type of print facilitates easy reading. The binding is well done, for which both the author and the publisher are to be congratulated.

The atlas is indispensable to the radiologist as a standard of comparison as well as to all physicians whose duty it is to interpret and treat traumatic and diseased states of the skeletal structures of the hand. The atlas is highly recommended without reservations.

Elements of Orthopaedic Surgery. By N. Ross Smith, Orthopaedic Surgeon, Cornelia Hospital, Poole, Australia, with foreword by R. C. Elmslie, Orthopaedic Surgeon, St. Bartholomew's Hospital. Cloth. Baltimore, 1937, William Wood and Company. $4.

The natural reaction that one has against small textbooks is quickly overcome on reading this work; and, although it is intended more for the general man and student than for the specialist, it can be read with profit by the latter also.

The field is covered in a remarkedly thorough way and, although the technique of treatment is not discussed in detail except in a few instances, the principles are well brought out and indications given. The chapter on postural deformities is excellent and the two chapters on fractures are concise and very well conceived.

The book can be recommended to all those interested in orthopedic surgery not only as a guide for further reading but also as a source of abbreviated but definite information on the subject.

Operative Surgery, the Ear, Air Passages and Neck. By Dr. Martin Kirschner (with the collaboration of A. Lautenschläger and O. Kleinschmidt). Authorized translation by I. S. Ravdin and George M. Coates. Pp. 528, with 460 illustrations. Philadelphia and London, 1937, J. B. Lippincott Company. $10.

This, the third volume in the operative surgery series of Professor Martin Kirschner, of Heidelberg, is worthy of the distinction of appearing on the shelf beside its two illustrious predecessors. This volume appears in two parts; the first relates to operations on the ear, the nose and its appendages, the pharynx, larynx, trachea, and bronchi. This section is written by Professor Lautenschläger, of Berlin, and is edited and translated by Dr. George M. Coates, of Philadelphia. Part Two concerns operations on the esophagus and other structures of the neck and is written by Professor Kleinschmidt, of Wiesbaden, and is edited and translated by Dr. I. S. Ravdin, of Philadelphia, who also sponsored the appearance of the first two volumes in English.

The approach to the description of operative procedures is distinctly anatomic. The influence of years of contact with cadaver surgery in the teaching of applied surgical anatomy to medical students, an exercise to which every academic German surgeon is thoroughly exposed, is immediately apparent. The anatomic plan of

operation so well elucidated by the authors is worthy of careful study. Physiologic considerations relating to the operations described, however, are often totally ignored by the writers. In the section on the neck, some of the obvious omissions have been repaired in part by the insertion of short pertinent sentences by the editor.

The illustrations, of which there are a large number, are beautifully done in color and add much to the effectiveness of the descriptions. How often American authors have occasion to be envious of their continental colleagues whose publishers permit them to use illustrations in color so generously.

A serious omission, the reviewer feels, is failure to append a satisfactory bibliography. Scores of names (largely German) are cited throughout the volume, but where these references are to be found is not intimated. The usefulness of the volume would have been increased several fold to the critical student of surgery by the proper insertion of suitable references.

The volume can be whole-heartedly recommended to any serious student of surgery having an interest in the subject matter.

Megacolon und Megacystis. By H. W. Passler. Unbound. Pp. 172, with 67 illustrations. Leipzig, 1937, Johann Ambrosius Barth, Publisher. 15.60 RM.

This little volume brings together more information on the subject of megacolon than has been assembled previously. It deserves to be read and studied widely. It summarizes authoritative information concerning the origin and treatment of megacolon. The author recognizes a "symptomatic," and "idiopathic" megacolon. He observes that idiopathic dilatation of the bladder attends idiopathic megacolon occasionally.

The well-known papers of Ask-Upmark, Anschütz, Konjetzny, Lehmann, and Neugebauer on the subject of Hirschsprung's disease are reviewed. Among direct attacks upon the diseased segment of the bowel, the author favors exteriorization and resection of the colon, although he admits that the lower portions of the pelvic colon cannot be removed by this method. Yet the remote as well as the immediate (lower mortality) results appear to be better by this method than by the one-stage resection. The suggestion of Wade and Royle to perform ramisection for this disorder has superseded all other operative procedures, however in the relief of megacolon when a demonstrable mechanical obstruction is not present. Of the operative attacks upon the sympathetic nervous system for the relief of obstipation attending megacolon, the bilateral lumbar ganglionectomy of Adson appears to give better remote results than do the more limited operations of Learmonth or the unilateral extraperitoneal excision of the left lumbar sympathetic chain.

There are two inaccuracies to be corrected, which do not invalidate the value of this important monograph, which should be called to the reader's attention: (1) The writer describes exteriorization of the pelvic colon as the Mikulicz procedure, which it is not. True, Mikulicz did a good deal to popularize this mode of operation when he first described it in 1903 (Arch. f. Chir. **69**: 29, 1903) in reporting cases of his own. Yet, Bloch, the Danish surgeon, had described it well as early as 1892 (Nord. med. Ark. **2**: 1, 1892). (2) The upside-down position in determining the extent of imperforation or atresia of the anal canal and rectum by roentgenography which the author ascribes to Zenker (Chirurg. **6**: 370, 1934) was first described by Wangensteen and Rice (Ann. Surg. **92**: 77, 1930).

The text is accompanied by a complete and useful index. The text can be recommended highly to anyone who has an interest in this subject.